COPYRIGHT DEPOSIT.

Volume V MARCH 1944 Number 3

DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

PUBLISHED MONTHLY for the PHYSICIAN in the GENERAL PRACTICE OF MEDICINE

CONTENTS:

THE DIAGNOSTIC VALUE OF DISTURBANCES OF CONSCIOUSNESS ..... Page 69
Jurgen Ruesch, M.D., Boston, Massachusetts

DELVINAL SODIUM VINOBARBITAL IN THE TREATMENT OF EPILEPTIC STATES ..... Page 84
Eugene Davidoff, M. D., *and*
George M. Doolittle, M.D., Sonyea, N. Y.

ELECTROENCEPHALOGRAPHIC STUDY DURING EPILEPTIC SEIZURES RELATED TO HYPERVENTILATION ..... Page 87
Leon J. Robinson, M.D., Palmer, Massachusetts

NEUROLOGICAL CLINICAL-PATHOLOGICAL CONFERENCE ..... Page 90

SANITARIA

The Library of Congress
Serial Record
MAR 9 1944

ASSOCIATE EDITORS

PETER BASSOE, M.D. ..... Chicago, Illinois
A. E. BENNETT, M.D. ..... Omaha, Nebraska
FRANCIS J. BRACELAND, M.D. ..... Philadelphia, Penn.
FRANKLIN G. EBAUGH, M.D. ..... Denver, Colorado
TEMPLE FAY, M.D. ..... Philadelphia, Penn.
HAMILTON FORD, M.D. ..... Galveston, Texas
WALTER FREEMAN, M.D. ..... Washington, D. C.
JAS. K. HALL, M.D. ..... Richmond, Virginia
GEORGE T. HARDING, M.D. ..... Columbus, Ohio
A. HAUSER, M.D. ..... Houston, Texas
LOUIS J. KARNOSH, M.D. ..... Cleveland, Ohio
JACOB KASANIN, M.D. ..... San Francisco, California
FRANK H. LUTON, M.D. ..... Nashville, Tennessee
WM. MALAMUD, M.D. ..... Worcester, Massachusetts
KARL A. MENNINGER, M.D. ..... Topeka, Kansas
ADOLF MEYER, M.D. ..... Baltimore, Maryland
GLENN MYERS, M.D. ..... Los Angeles, California
HANS H. REESE, M.D. ..... Madison, Wisconsin
PAUL L. SCHROEDER, M.D. ..... Chicago, Illinois
THEODORE A. WATTERS, M.D. ..... New Orleans, La.
S. BERNARD WORTIS, M.D. ..... New York, N. Y.

TITUS H. HARRIS, M.D.
Galveston, Texas
EDITOR-IN-CHIEF

YEARLY SUBSCRIPTION $2.50
SINGLE COPIES 25 Cents

GEORGE BERGEIR, B.S., LL.B.
Chicago, Illinois
MANAGING EDITOR

MAR -8 1944

THE
RING SANATORIUM AND HOSPITAL
Arlington Massachusetts

Eight miles from Boston at an elevation of 400 feet

63rd Year

Specializing in the individualized care of Neuropsychiatric illnesses and Habit conditions. All accepted Therapies under the direction of a resident medical staff and trained assistants. Cottage plan permits a variety of accomodations.

VOLTA ROSS HALL, M.D.
Medical Director

HALLAM T. RING
Administrator

In conjunction: The Ring School of Psychiatric Nursing

THE HARDING SANITARIUM WORTHINGTON, OHIO

For Nervous and Mental Disorders

NINE MILES NORTH OF STATE HOUSE—COLUMBUS

GEORGE T. HARDING, M.D., *Medical Director*
HARRISON EVANS, M.D.

FRED H. WEBER, M.D.
MARY J. WEBER, M.D.

COMPTON SANITARIUM
AND
LAS CAMPANAS HOSPITAL

COMPTON, CALIFORNIA
(Near Los Angeles)

Compton Sanitarium is a private psychiatric hospital with 120 beds. Emphasis is given psychotherapy by a staff of resident psychiatrists. Other treatment procedures are duly evaluated and administered. Careful records are maintained. There are psychiatrically trained graduate nurses; student nurses through affiliation; nursing attendants; dietitian; occupational therapist; recreational therapist; hydrotherapist; masseuse. Las Campanas Hospital (43 beds) provides adjunct general hospital facilities. Compton Sanitarium and Las Campanas Hospital are approved by the American College of Surgeons.

GLENN MYERS, M.D.
Medical Director.

Beverly Hills Sanitarium

for

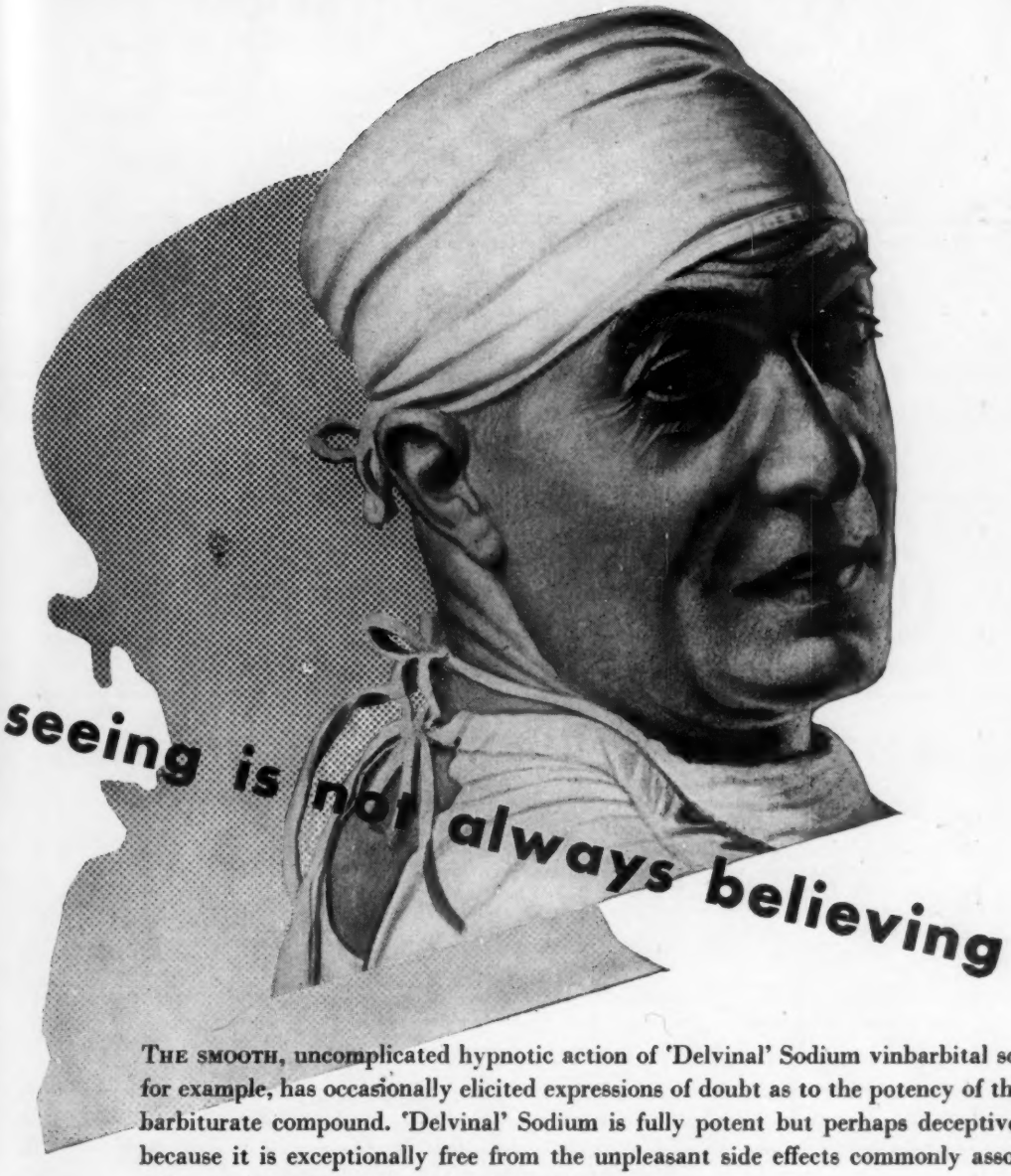
The Study and Treatment of Nervous and Mental Diseases

218 No. Westmoreland DALLAS, TEXAS Telephone 9-3114

This sanitarium is a psychopathic hospital with a home-like environment and is equipped to treat psychiatric and neurological cases in a most scientific manner by means of psychotherapy, occupational therapy, recreational therapy and physiotherapy, including hyperpyrexia, insulin and metrazol treatments in special conditions.

ARTHUR J. SCHWENKENBERG, M.D.
Attending Neuropsychiatrist

ROBERT E. WINN, M.D.
Resident Physician



THE SMOOTH, uncomplicated hypnotic action of 'Delvinal' Sodium vinbarbital sodium, for example, has occasionally elicited expressions of doubt as to the potency of this new barbiturate compound. 'Delvinal' Sodium is fully potent but perhaps deceptively so, because it is exceptionally free from the unpleasant side effects commonly associated with administration of sedative-hypnotic drugs.

The emotional strain of war-time living has caused a noticeable increase of functional insomnia, for the relief of which 'Delvinal' Sodium is ideally suited. A single dose of 1½ to 3 grains is generally sufficient to induce sound, refreshing sleep without "drugged" sensations during induction or "hangover" upon awakening. 'Delvinal' Sodium vinbarbital sodium is also indicated as a sedative in certain psychiatric conditions, as well as for pre-operative sedation, pre-anesthetic hypnosis, and obstetric sedation and amnesia. This remarkably efficient preparation is supplied in distinctively colored capsules of three strengths: ½ grain (brown), 1½ grains (orange), and 3 grains (orange and brown). Sharp & Dohme, Philadelphia 1, Pa.

'DELVINAL' SODIUM

Vinbarbital Sodium

CHESTNUT LODGE SANITARIUM

An institution for the application of Psychoanalytic Psychiatry to the Psychoses and Psychoneuroses.

DEXTER M. BULLARD, M.D.
Physician-in-charge
Rockville — Maryland

Tucker Hospital

212 West Franklin Street (Corner Madison)
RICHMOND, VIRGINIA

A private hospital for the study and treatment of Neuropsychiatric and Endocrinological Cases

Under the Charge of
Drs. Beverley R. Tucker, Howard R. Masters, and Jas. Asa Shield

THE MARY E. POGUE SCHOOL

For Retarded or Exceptional Children

Children are grouped according to type, each in its own department, with separate buildings for boys and girls. Spacious and beautifully landscaped grounds. Five school rooms. Teachers are all college trained with Teachers' Certificates.
Occupational Therapy. Vocational Training. Speech Corrective Work.
The School is only 26 miles west of Chicago, on or near all west highways out of Chicago.
Referring physicians may continue to supervise care and treatment of children placed in the School.
Inspection is invited — Physicians may send for catalog.

90 Geneva Road, Wheaton, Ill. :: Phone: Wheaton 66

SAINT ALBANS SANATORIUM

RADFORD, VIRGINIA

For the diagnosis, care and treatment of Nervous and Mental Diseases and Alcoholism

For rates and further information, address
JAMES P. KING, M.D.

RAHM ELECTRO-SHOCK RECORDER

A newly developed combination of Electro-Shock Machine and Surge Current Recorder . . . Produces an instantaneous, permanent record of current administered as treatment is given . . . Compact, convenient unit, completely portable, safe and simple to operate . . . Variable timing (0.10, 0.20, 0.30, 0.40 seconds) at voltages from 0-150 volts.

Literature available upon request.

RAHM INSTRUMENTS, Inc.
12 West Broadway, New York, N. Y.

Manufacturers and Engineers of Electro-Medical Equipment.

RAHM ELECTRO-SHOCK MACHINES
RAHM ELECTRO-ENCEPHALOGRAPHS
RAHM ELECTRO-STETHOGRAPHS
RAHM CORTICAL STIMULATORS

The LIVERMORE SANITARIUM — Livermore, California

SAN FRANCISCO OFFICE—450 SUTTER STREET

FOR NERVOUS AND MENTAL DISEASES

Situated in a beautiful valley forty miles from San Francisco. two hours ride on the Southern Pacific Railroad. Elevation five hundred feet. Climate excellent with sunshine almost every day.

Large resident medical staff; Well trained nursing service; Clinical Laboratory; X-ray department; Hydrotherapy, Athletic and Occupational Departments. Dietary Department insures an excellent cuisine.

Separate Department for the functional neuroses. Cottage system for mental patients.

Several Bungalows for individual patients. wishing home-like surroundings with absolute privacy and the very best accommodations.

Booklet on request.

J. W. Robertson, M.D., Consulting **Clifford W. Mack, M.D., Superintendent**

SAINT JOSEPH SANITARIUM

(Supervision of Sisters of Mercy)
P. O. Box 236
Dubuque, Iowa
or phone 526 for information
Mild Mental and Nervous Cases
also
Rheumatism, High Blood Pressure, Neuritis, Obesity, and all Types of Convalescents
Modern Hydrotherapy, Baths and Massage
Insulin Therapy Resident Physician

FENWICK SANITARIUM

COVINGTON, LOUISIANA

For Mild Mental and Nervous Cases as well as the Addiction Diseases.

In continuous operation for over fifty years.

For full information write, DR. F. F. YOUNG, *Director*

Rogers Memorial Sanitarium

OCONOMOWOC, WISCONSIN

Telephone 448

A PRIVATE sanitarium (incorporated not-for-profit)

for the treatment of

Diseases of the Nervous System

All approved methods of therapy are used

Resident Physicians

JAMES C. HASSALL, M.D. — *Medical Director*

CHARLES H. FEASLER, M.D.

An Institution for the study and treatment of Nervous and Mental Disorders.

Write for booklet.

JOHN H. NICHOLS, M.D., *Medical Director**
R. R. GOULD, M.D., *Acting Resident Director*

EST. 1898

*Military Leave of Absence

HERBERT A. SIHLER, *Director*
EDMUND V. SIHLER, *Assistant Director*

WINDSOR HOSPITAL

CHAGRIN FALLS, OHIO • Phone: Chagrin Falls 7347

Member American Hospital Association and Central Neuropsychiatric Hospital Ass'n.

NORTH SHORE HEALTH RESORT

WINNETKA, ILLINOIS

On the Shores of Lake Michigan

- **Homelike Environment**
- **Attractive Furnishings**
- **Spacious Landscaped Grounds**
- **Moderate Rates**

A completely equipped Sanitarium for the care of nervous and mental disorders, alcoholism and drug addiction, offering all forms of treatment, including electric and insulin shock.

Attractive restful surroundings for convalescents.

SAMUEL LIEBMAN, M.S., M.D.

Medical Director

225 Sheridan Road — ***Phone Winnetka 211***

VOL. V MARCH 1944 No. 3

EDITORIAL OFFICES
UNIVERSITY OF TEXAS SCHOOL OF MEDICINE
800 AVENUE B., GALVESTON, TEXAS

BUSINESS OFFICES
PHYSICIANS POSTGRADUATE PRESS
500 NORTH DEARBORN ST., CHICAGO 10, ILLINOIS

COPYRIGHT, 1944 BY
PHYSICIANS POSTGRADUATE PRESS

DISEASES of the NERVOUS SYSTEM

(PUBLISHED MONTHLY)

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

The Diagnostic Value of Disturbances of Consciousness*

JURGEN RUESCH, M.D.
Boston, Massachusetts

The present study, concerned with the diagnostic value of disturbances of consciousness, is based on 49 clinically examined patients and on 286 cases with a history of repeated or prolonged disturbances of consciousness in which postmortem examinations of cranial cavity and brain had been performed. One of the common features of conditions such as coma, semicoma, stupor, delirium, confusion, sensory aphasia, drowsiness and severe intellectual impairment is the absence of adequate and correct awareness of the environment due to impairment of brain functioning. For practical medical purposes these allied states can be called disturbances of consciousness, without touching the controversial topic of psychological and philosophical interpretations of the term consciousness itself.[1]

Review of the recent literature revealed that a great many relevant observations have been reported, but that very few studies dealt with the similarity of these disturbances. Bissel and Le Count,[2,3] Holcomb,[4] and Solomon and Aring[5,6,7] reported about frequency, causes and diagnosis of comatose conditions. Clinical aspects of coma, delirium and allied states have been discussed by Wolf and Curran,[8] Purves-Stewart,[9] Bailey[10] (confusion and stupor), Hill[11] (cardiovascular disorders), Garland[12] (infections and neoplastic diseases), and Oakley[13] (diabetes and uremia). Denny-Brown and Russel,[14] Northfield,[15] Ruesch and Moore,[16,17] and others reported about unconsciousness in head injuries. The diagnostic value of aphasia and agnosia has recently been stressed again by Nielsen[18] and intellectual impairment was a topic of a great number of publications, Roe and Shakow,[19] Ruesch,[16] and others. Discussions dealing with the problem of unconsciousness in general were given by Jahrreiss,[20] Penfield,[21] and Cobb.[22,23] Bleuler[24] emphasized the "organic syndrome" as the common and outstanding feature of brain disease, but he confined it primarily to disturbances of memory, orientation, apperception, and affects. Yet everyone is familiar with progressive brain diseases such as tumors, senile and arteriosclerotic conditions, subdural hematomas, Schilder's disease and others in which defects of memory may be the first signs to attract attention. Later more profound confusion or delirium, often leading through a transitional stage of stupor, may ultimately result in coma and death. The reverse sequence can be observed in patients with head injuries,[16,17] intoxications, anesthesia,[25] electric, metrazol,[26] or insulin shock[27] in which coma is followed by semicoma and stupor. Later on, an intermediary period of confusion may be observed which results frequently in temporary psychological impairment before full health is regained.[16]

The above observations definitely suggest that there exists a common background for these successive stages of brain disease. A

*From the Psychiatric Department of the Massachusetts General Hospital and the Department of Neuropathology of the Harvard Medical School.

This study has been made possible by a grant from the Josiah Macy Jr. Foundation.

series of neurophysiological and biochemical studies indicate that in the majority of disturbances of consciousness, the arteriovenous difference in the oxygen content of the cerebral blood is diminished,[28,29,30,31,32] the electrical activity of the brain abnormal,[33,34] and the cerebral circulation altered.[17,35] In view of those findings, it seemed worth while to investigate whether the clinical aspects of a variety of diseases would not have many features in common and whether a method could be found which would lend itself for the examination of all stages of unconsciousness. Once the degree of the disturbances could be measured, it seemed of further interest to determine the diagnostic value of the various types of unconsciousness. The present study therefore reports results obtained with a standardized clinical examination method as well as diagnostic criteria derived from the analysis of autopsy records of patients who suffered from disturbances of consciousness.

Clinical Study

Method—In order to examine a variety of cerebral functions in progressive stages of brain disease, tests were considered with the intent to cover the whole range from primitive to the most complex functions. Elementary reflexes, higher reflexes controlled by voluntary action, verbal or written statements regarding the degree of the patient's awareness of the surroundings and finally examination of the intellectual functions were included: *(see table below.)*

The majority of the above named phenomena are well known; some of the tests, however, may need further comments:

Reaction to noise—Sudden noise, such as unexpected handclap behind the patient's ear, may result in several reactions. Reactive movements of the head or body indicate that the sound was perceived. Often the eyes or the head, or both, may turn towards the source of the noise, or the subject may blink.[14]

Reaction to visual threats—The reflex is elicited by suddenly moving an object or the finger towards the subject's eye without touching it. Blinking indicates perception of the approaching danger.[36]

Reaction to verbal commands—The ability to execute simple commands, such as shutting the eyes or sticking out the tongue, depends on several factors. The subject has to understand spoken or written language, and must not suffer from aphasia or agnosia. He must be willing to cooperate and to pay attention to instructions; coherence of the mental processes is, therefore, necessary to elicit appropriate responses.

Voluntary suppression of the light-lid reflex—This reflex is elicited by suddenly bringing a bright light close to the eye, whereupon the subject either blinks or shuts his eyes tightly. Fully conscious patients can be instructed beforehand to keep their eyes wide open and to overcome their desire to shut the eyes in presence of the light. Semi-conscious subjects cannot overcome this desire, and unconscious patients manifest no reaction at all.

Optico-kinetic nystagmus—It occurs when successive moving objects cross the field of vision. Also known under the names of optical rotatory nystagmus and optico-motor nystagmus, this phenomenon is produced by the attempt of the eye to follow a moving object until it reaches the peripheral field, causing a slow outward movement of the eye; when the attention is attracted by another object, the eye jerks back rapidly. The instrument

Elementary Reflexes	*Higher Reflexes*	*Awareness of the Surroundings*	*Higher Intellectual Functions*
Plantar or dorsal flexion	Reaction to being called by name	Orientation with regard to self	Insight into present situation
Pupillary light reflex	Reaction to noise	Orientation for place	Ability to submit to psychological testing
Withdrawal of leg following pin prick	Reaction to visual threat	Orientation for time	Memory for recent events
Corneal reflex	Reaction to verbal commands		
Knee jerk	Voluntary suppression of the light-lid reflex		
	Optico-kinetic nystagmus		
	Fixation reflex		

used to elicit nystagmus[37] consists of a vertical drum about 12 inches in height and 8 inches in diameter. A central rod is fitted through the drum's vertical axis so that it may be revolved slowly. A suitable handle is placed just underneath the drum into which the center rod may be fastened. Nystagmus may be induced by turning the drum slowly. It is extremely difficult for a seeing person to avoid looking at the device, and when he does so, nystagmus will result.[38,39]

The fixation reflex—When a light falls upon a peripheral part of the retina and is appreciated by consciousness, the eyes are reflexly moved in such a way that the image falls upon the fovea. Subjects with disturbances of consciousness are unable to fix a moving finger or flashlight.

Ability to submit to psychological testing results from the presence of a number of factors such as coherence of thinking, desire to cooperate, and attention paid to what is said. The following three tests are used: Pictorial Absurdities and Verbal Absurdities, out of the Wells-Ruesch Manual,[40] and serial subtractions of 7 from 100. It should be noted that test scores are not an issue in this item. Instead, the interest is focused on the patient's ability to submit to examination, to understand the instructions, and to give it a trial. Hence it can be considered a measure of rationality.

Case Material—A group of 49 hospitalized and unselected patients in care of neuromedical, neurosurgical, psychiatric, medical or surgical services, suffering from disturbances of consciousness ranging from deep coma to slight confusion and residual intellectual impairment were studied. The mean age of the subjects was 46, ranging from 8 to 72 years. There were 34 males and 15 females. The diagnostic distribution of the cases was as follows: Head injuries 9, brain tumors 9, cerebral vascular accidents 6, convulsive disorders 4, abdominal malignancies 3, thoracic malignancies 3, anemias and leukemias 3, drug intoxications 3, diabetic comas 3, cardiac diseases 2, hepatic diseases 2, meningitis 1, thyrotoxicosis 1.

Data—In Figure 1 the results of 72 different examinations of 49 patients are given under the heading of "Signs of Consciousness."

The data are presented in terms of examinations rather than in terms of cases because some of the patients were examined repeatedly whenever they showed a progression of the disease and a change in the level of consciousness. Each correct response, be it of reflex or psychological nature, is marked x. Blank spaces thus indicate that the response is either defective (present on one side only) or entirely absent. In the left hand columns it was noted whether the patients were subjected to any type of sedation 24 hours prior to the examination. The note concerning recovery informs the reader of the outcome and hence the severity of the disease. Defective recovery is indicated by a psychological test performance which falls below the estimate of an individual's capacity as obtained from educational or occupational history.[16] The remark about changes in vital signs is based on the presence of abnormalities of temperature (above 100°), pulse rate (above 100 and below 60), respiratory rate (above 25 and below 15), and blood pressure (above 180 and below 80 systolic). Examinations 53 to 72 were done on patients who previously had been in coma, and who by that time had only residual intellectual defects.

The data have been arranged from left to right according to increasing numbers of correct responses obtained. The sequence from top to bottom corresponds to a decreasing order of severity of the disturbance. Fig. 1, therefore, indicates that there exists a lawful progression in the number and type of signs involved the severer a disturbance of consciousness becomes. In this diversified series of diseases, the ability to establish memory traces, to undergo psychological testing, to show judgment and insight into the situation and orientation in time is usually first and most frequently disturbed. Changes in vital signs and death rate are low and recovery is likely to occur, though with deficiency. The signs which fail next are orientation for place and person, the ability to fix an object with the eyes and the optico-kinetic nystagmus. Failure to execute commands and deficiency of the noci-ceptive reflexes follow next. Absence of these signs is already associated with a high percentage of changes in vital signs and a high death rate. Recovery is unlikely and necessity for sedation rather frequent. The last of the higher functions to disappear is the reaction to call by name. This and the

absence of reflexes is an ominous sign, since changes in vital signs and death are the rule.

Pathological Study

Method—The study was confined to "prolonged" and "repeated" disturbances of consciousness for technical reasons. Most patients have short periods of coma, semicoma, or confusion prior to death, which are often not especially mentioned in hospital records. Repeated or protracted episodes of unconsciousness, however, are apt to be listed as conspicuous clinical signs. "Prolonged" disturbances were arbitrarily defined as phenomena of longer than 72 hours' duration. "Repeated" was used to describe any occurrence of unconsciousness from which the patient recovered before dying in the terminal coma. Through the courtesy of the department of pathology of the Massachusetts General Hospital, 286 cases were collected which fulfilled the criteria of prolonged and repeated disturbances of consciousness. To find these it was necessary to review 1682 autopsy protocols in which the brain had been subjected to macroscopic and microscopic examination. These, in turn, derived from 4000 restricted and incomplete autopsy reports, cov-

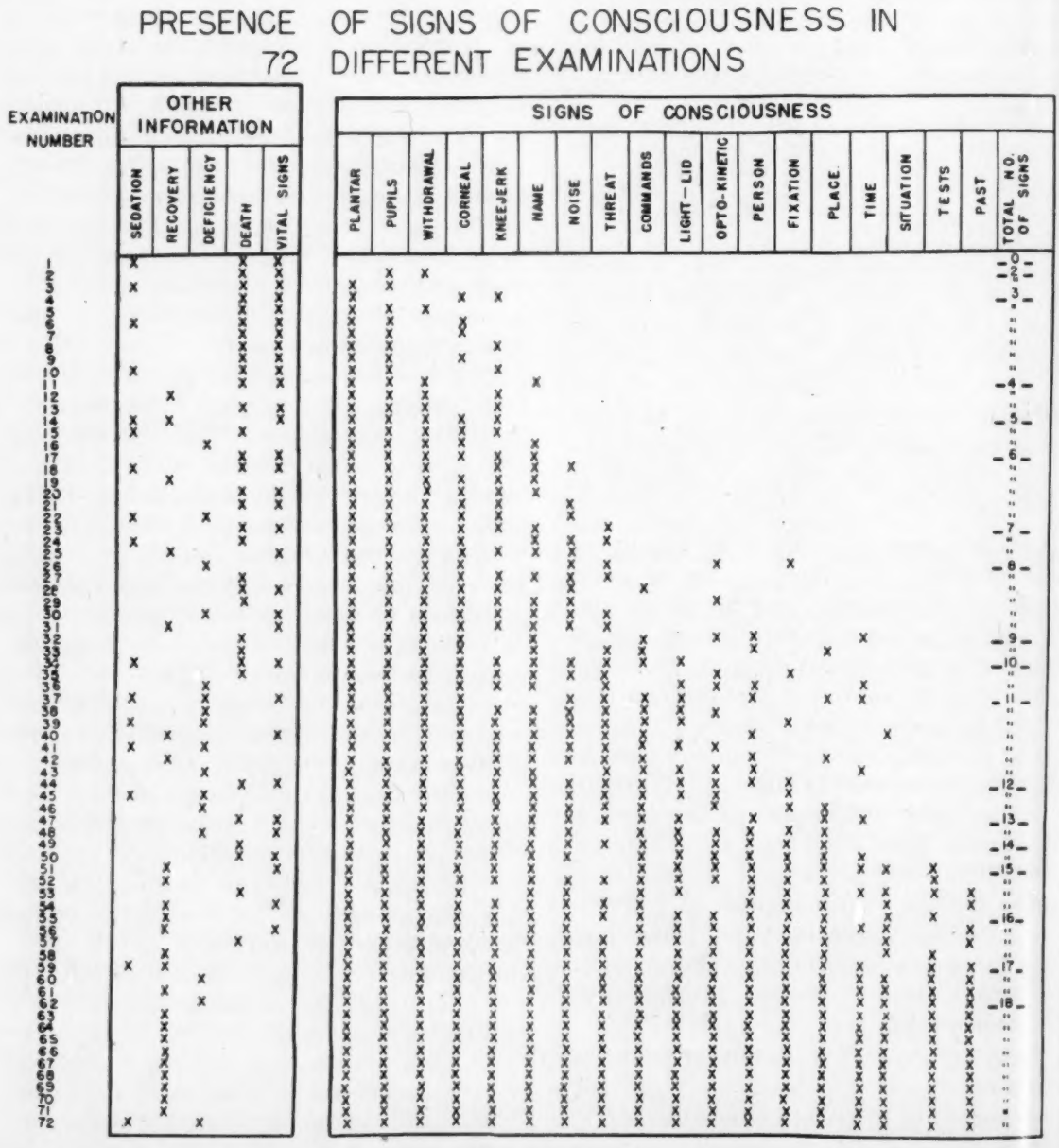


FIGURE 1

ering a period of approximately 10 years. The autopsy material was supplied by the divisions of Medicine, Surgery, Pediatrics, Neurology, Neurosurgery, Psychiatry, and the McLean Hospital for Mental Diseases, thus assuring a diversified representation of diseases. The clinical information was obtained from the carefully prepared abstracts of each case, some of which are published weekly in the New England Journal of Medicine. When necessary, the data were completed by information from the original hospital records. Review of the clinical data revealed that the disturbances met in this series could be classified into 13 categories, the criteria of which are given on page 77. The evaluation of the autopsy protocols was done from a clinical viewpoint. Age and sex of the patients, duration and cause of the disturbance, gross classification of the pathological findings and brain regions affected were in the center of the investigation. Histological details and individual cases were not reported since they do not lend themselves for statistical treatment which is necessary to determine the diagnostic value of various disturbances. In order to avoid arbitrary classifications, cases with more than one type of disturbance, such as repeated convulsions in addition to a prolonged coma, had to be listed twice (69 cases) so that the sum of the cases in each category adds up to 355, exceeding the total of 286 autopsies. The same procedure was adopted in the treatment of the neuropathological findings, and in the study of the frequency of localized lesions.

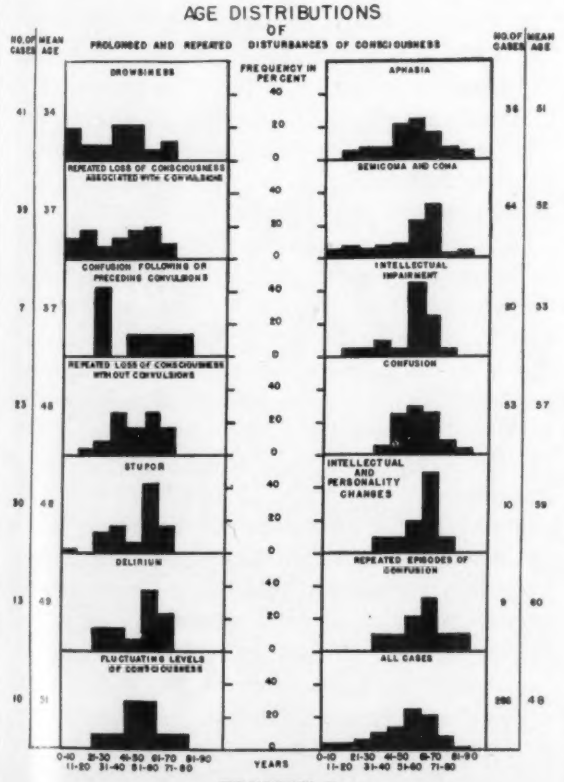


FIGURE 2

Data

The disturbances of consciousness are arranged in increasing order of mean ages. The distribution curve of all the 286 cases indicates that the peak of occurrence of disturbances of consciousness is in the age group 51-60, followed by the seventh, and then by the fifth and fourth decades. The following points are of especial interest: Prolonged comas and semicomas and, to a less degree, aphasias, cover a wider age range than do the other disturbances. Intellectual impairment and confusional states are rare before the age of 30. Delirium, aphasia, and stupor occur infrequently in the first two decades.

TABLE I

SEX DISTRIBUTIONS OF PROLONGED AND REPEATED DISTURBANCES OF CONSCIOUSNESS

Type of disturbance	*No. of cases*	*Sex incidence in per cent*	
		Males	*Females*
Delirium	13	92	8
Intellectual and personality changes	10	80	20
Prolonged confusion	53	76	24
Intellectual impairment	20	75	25
Confusion following or preceding convulsions	7	71	29
Repeated episodes of confusion	9	67	33
Aphasia	36	67	33
Repeated loss of consciousness associated with convulsions	37	54	46
Prolonged drowsiness	41	49	51
Prolonged semicoma and coma	64	47	53
Repeated loss of consciousness without convulsions	23	43	57
Prolonged stupor	30	43	57
Fluctuating levels of consciousness	10	40	60
All cases	286	59	41

Intellectual impairment, confusional states, and aphasias seem to be more frequent in males; coma, repeated coma, stupor, and fluctuating levels of consciousness more frequent in females. The group with convulsions and drowsiness has an equal sex distribution.

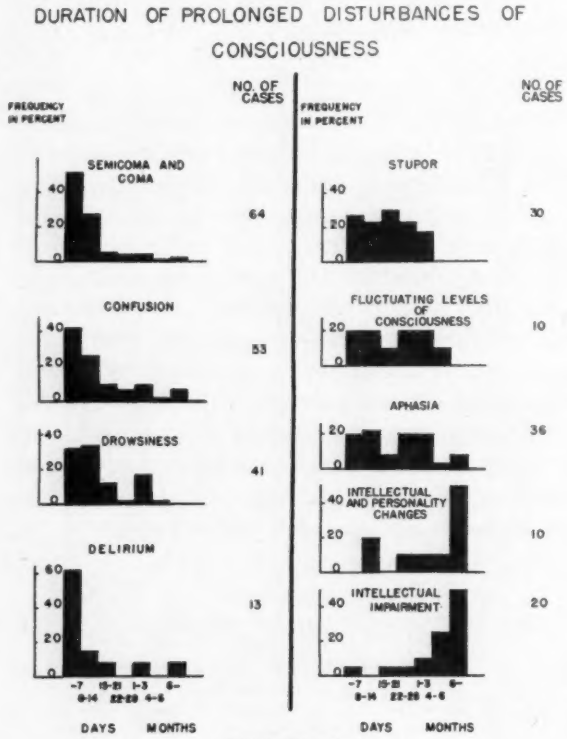


FIGURE 3

This picture is arranged in order of increasing duration of disturbances of consciousness. The distribution curves reveal that though most of the disturbances last from a few days to several months, coma, confusion, drowsiness, and delirium are usually short disturbances of one or two weeks' duration. The majority of the stupors last three weeks and a large percentage of cases with fluctuating levels of consciousness and aphasia last over a month. The intellectual and personality disturbances claim the longest duration and usually last longer than 6 months.

Table 2 gives the percentage distributions for all the categories of disturbed consciousness, arranged in vertical columns from top to bottom. Thus under intellectual impairment, for instance, are listed the detailed figures which are responsible for the total occurrence of diffuse cerebral, meningeal, vascular, infectious and neoplastic pathology. Though the majority of the terms used are self-explanatory, the following comments seem to be necessary: Cerebral atrophy refers to macroscopic findings such as widening of the sulci, atrophic convolutions, enlarged ventricles, and low brain weight. Cerebral degeneration describes cases in which microscopic evidence of degeneration can be found. Examples of such findings are: thinning out of the cortex; disorganization of the cortical architecture; acute swelling of the ganglion cells; sclerotic, pyknotic, and ischemic changes; destruction of myelin and axis cylinders; and proliferation or degeneration of glia cells. The term "miscellaneous" under diffuse cerebral pathology includes the slight abnormalities found in cases of edema of the brain, in uremia, and in other toxic conditions where the findings are definite but minimal; for example, swollen ganglion cells, areas in which the staining is darker or paler than usual, changes in the Nissl bodies without actual destruction of ganglion cells, swelling of astrocytes without increase in number, etc. The category encephalitis includes only those conditions in which inflammatory cells (polymorphonuclears, lymphocytes, plasma cells, etc.) can be found in the perivascular spaces or in substances of the brain. Cases of general paresis are included in this category. The vascular findings were classified according to the mechanism of the disturbance such as embolism or thrombosis. The category of infarcts and softening includes all those findings in which the vascular mechanism remained unknown. This was especially the case in old or very small lesions.

Considering the distributions of the neuropathological findings, the following observations seem to be relevant: Diffuse cerebral and vascular pathology occur in all types of disturbances of consciousness. Vascular findings are the most frequent (54 per cent), diffuse and neoplastic pathology follows next (28 per cent each), while diffuse meningeal findings (15 per cent), localized infection (7 per cent), and extracerebral pathology only (5 per cent) come last. Meningeal pathology, however, is absent in intellectual impairment and in intellectual and personality changes, in repeated episodes of confusion, and in confusion following convulsions. Brain and subdural abscesses are absent in intellectual impairment, in intellectual and personality changes, in delirium, in fluctuating levels of

TABLE 2

FREQUENCY OF NEUROPATHOLOGICAL DIAGNOSES IN PROLONGED AND REPEATED DISTURBANCES OF CONSCIOUSNESS

Category	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV
Number of Cases	20	10	53	13	41	10	36	30	64	7	9	23	39	286
	Intellectual Impairment	Intellectual and Personality Changes	Confusion	Delirium	Drowsiness	Fluctuating Levels of Consciousness	Aphasia	Stupor	Semi-coma and Coma	Prolonged Confusion Following or Preceding Convulsions	Repeated Episodes of Confusion	Repeated Loss of Consciousness Without Convulsions	Repeated Loss of Consciousness Associated With Convulsions	All Cases
	Frequency in Per Cent													
Diffuse Cerebral Pathology														
Cerebral Degeneration	15	20	17	23	17	20	11	20	11	29	33	9	16	14
Cerebral Atrophy	5		17	8	5	10	6	3	5		11	13		6
Schilder's and Alzheimer's Disease	15		4				6		3				11	2
Encephalitis	10		4		5		6						5	3
Miscellaneous		10	2		7				2			4	5	3
Total	45	30	44	31	34	30	29	23	21	29	44	26	37	28
Diffuse Meningeal Pathology														
Meningitis and Meningeal Metastases			7	50	24	10	11	13	16			8	18	15
Localized Pathology in Brain and Meninges														
Vascular:														
Small Infarcts and Softenings	25	10	25	15	12	40	36	23	11	14	34	17	3	22
Arterial, Intracerebral Hemorrhage	15	20	4		12	10	8	17	11	14	33	17	5	10
Arterial Thrombosis	5		4		5	10	17	7	9	29	33	4	5	5
Arterial Embolism	5		4			20	3	7	9			22		4
Sinus and Veinous Thrombosis				8	12		11	3	5			13		5
Sub- and Epidural Hemorrhage					5	10	3	7	6			9	3	4
Subarachnoid Hemorrhage			2		10			10	3			9		4
Total	50	30	39	23	56	90	78	74	54	57	100	91	16	54
Infectious:														
Brain Abscess			2		10		3	7	5	14		4	5	5
Subdural Abscess			2		2		3	3	3				5	2
Total			4		12		6	10	8	14		4	10	7
Neoplastic:														
Glioblastoma Multiform	20	20	9		7	10	25	13	19	14			8	12
Other Gliomas	15		10		12		6	7	6			4	19	6
Metastatic Tumors		20			7	10	11	7					3	5
Hemangiomas & Hemangioblastomas			2		2				3				8	2
Meningiomas	5		1		2	10	3	3				4	3	2
Pituitory Tumors & Craniopharyngiomas					2							4	3	1
Total	40	40	22		32	30	45	30	28	14		12	44	28
Extra Cerebral and Extra Meningeal Pathology														
Findings in Arteries Only					5			7	5				5	4
No Findings at All	5		6	15		10		7						3
Atrophy of Pituitary. Pathology in Falx and Skull					2					14		4		1
Total	5		6	15	7	10		14	5	14		4	5	8

consciousness, and in prolonged confusion following convulsions. Tumors could not be found in deliria or in repeated episodes of confusion.

An attempt was made to evaluate cerebral and extra-cerebral autopsy findings with regard to the causes which lead to the disturbances of consciousness. Under toxic causes were included exogenous poisonings as well as autointoxications, such as uremia. Infectious conditions comprise bacillary, as well as virus infections (influenza, syphilis, tuberculosis, strepto-staphylo, meningo-, and pneumococcic infections, exclusive of infections of the endocardium). Neoplastic diseases include all brain, meningeal, and metastatic tumors. Endocrine diseases comprise Simmond's disease, thyrotoxicosis, diabetes, etc. Blood diseases include all anemias and leukemias. Endocardium diseases of arteriosclerotic, rheumatic, and bacterial origin were listed separately, since they frequently cause cerebral embolism. Arteriosclerosis comprises all the cases in which the findings were probably caused by cerebral or extra-cerebral arteriosclerosis or by essential hypertension. Cerebral aneurysms were found in a number of cases where death was due to subarachnoid and intracerebral hemorrhage. The category miscellaneous and unknown includes rare conditions, such as one case of cerebral periarteritis nodosa, and those cases where no satisfactory explanation could be found. These conditions were: Alzheimer's and Schilder's disease, cerebral degeneration of unknown cause, and others.

Considering the distribution for all the cases, one finds that disturbances of consciousness are usually caused by tumors (27 per cent), infections (22 per cent) or arteriosclerotic conditions (20 per cent). Miscellaneous conditions (9 per cent), endocardial diseases (8 per cent), toxic conditions (5 per cent), aneurysms (5 per cent), endocrine disorders (2 per cent), and blood diseases (2 per cent) belong to the less frequent causes.

All the cases showing single or multiple focal lesions were analyzed with regard to the frequency of occurrences of affected brain regions. The overall distribution indicates that there is no predilection for either left or right side. The basal ganglia (including the hypothalamus) show the highest inci-

TABLE 3

PROBABLE CAUSES OF PROLONGED AND REPEATED DISTURBANCES OF CONSCIOUSNESS

		Frequency in Per Cent								
	Number of cases	*Neoplasms*	*Infections*	*Arteriosclerosis*	*Diseases of endocardium*	*Toxic conditions*	*Aneurysms*	*Endocrine Diseases*	*Blood diseases*	*Miscellaneous*
Intellectual impairment	20	40	15	20	5					20
Intellectual and personality changes	10	40		20						40
Confusion	53	23	15	32	11	2	2		4	11
Delirium	13		69	15	8	8				
Drowsiness	41	34	27	2	2	12	10			12
Fluctuating levels of consciousness	10	30	20		30		10	10		
Aphasia	36	41	21	19	8	3				
Stupor	30	30	13	17	3	10	10	3		13
Semicoma and coma	64	27	27	22	11	6	3		2	3
Prolonged confusion following or preceding convulsions	7	14	14	29	14		14			
Repeated episodes of confusion	9		11	67	11					
Repeated loss of consciousness without convulsions	23	13	9	26	32	4	9	9		8
Repeated loss of consciousness with convulsions	39	41	25	8		8	3		5	10
All cases	286	27	22	20	8	5	5	2	2	9

dence (20 per cent) due to the fact that left and right-sided lesions were considered together in one group. The temporo-parietal regions (15 and 17 per cent) and the frontal region with 11 and 12 per cent follow next. The other parts of the brain are less frequently affected.

Characteristic Features of Disturbances of Consciousness

The following summary contains the definitions of the disturbances studied, as well as the characteristic aspects found in the analysis of age, sex, duration, neuropathology, causes of the disease and localization of the lesions.

I. *Intellectual impairment* includes disturbances of memory and judgment with undisturbed orientation in absence of hallucinations or illusions. It occurs predominantly in the age groups above 50. It affects males more often than females and, when it occurs, it usually lasts months or years. The pathology found is either of diffuse cerebral, vascular, or of neoplastic origin. Tumors cause impairment more frequently than infections, arteriosclerosis, or unknown degenerative processes. The localization of the lesions is almost always in the hemispheres or in the basal ganglia.

II. *Intellectual and personality changes* designate in addition to the abnormalities mentioned above, recent difficulties in interpersonal relationships or changes of attitude, ideas of reference, delusions, and mood swings. The group is characterized by the same features as those outlined above. The age group is, however, slightly older, and in-

TABLE 4

FREQUENCY OF LOCALIZATION OF FOCAL LESIONS IN PROLONGED AND REPEATED DISTURBANCES OF CONSCIOUSNESS

		Frequency in Per Cent												
	Number of Cases	*Right Frontal Lobe*	*Left Frontal Lobe*	*Right Temporo-parietal Lobe*	*Left Temporo-parietal Lobe*	*Right Occipital Lobe*	*Left Occipital Lobe*	*Basal Ganglia*	*Corpus Callosum*	*Midbrain*	*Brain Stem*	*Cerebellum*	*Pressure Cones and Herniations*
Intellectual Impairment	20	15	10	25	15		5	30	5		15	5	
Intellectual and Personality Changes	10	10		20	10	10		10					
Confusion	53	9	8	13	11	9	4	25		4	8	6	6
Delirium	13		14					14					14
Drowsiness	41	10	12	12	20	2	2	24	2	7	12	7	12
Fluctuating Levels of Consciousness	10	10				10		30	10	10	10	10	
Aphasia	36	8	25	6	67	6	8	19	6	3	3	8	
Stupor	30	17	17	17	20	10	7	17	3	3	10	7	3
Semi-coma and Coma	64	16	20	22	22	9	11	27	6	2	5	6	3
Prolonged Confusion Following or Preceding Convulsions	7		29	29	29		14	57		14			
Repeated Episodes of Confusion	9	11		11	22	11	11	56					
Repeated Loss of Consciousness Without Convulsions	23	4	13	13	26	13	9	30			13	17	4
Repeated Loss of Consciousness Associated With Convulsions	39	20	13	18	16	3	8	13	5	3			3
All Cases	286	11	12	15	17	5	5	20	3	2	6	7	7

fectious processes could not be found as causes of the disturbance.

III. *Prolonged confusion* refers to a condition in which there is disturbed orientation as well as intellectual impairment. Cases described as "irrational" were included in this category. It occurs most frequently in the age groups above 40 and in males. Generally the duration is a matter of one or two weeks. The pathology is more often diffuse and vascular in character than of neoplastic nature. The predominant causes are arteriosclerosis, followed by tumors, infections, endocardial and degenerative processes. The localization of the lesions is scattered all over the brain with a slight predilection for the basal ganglia.

IV. *Prolonged delirium* is a state of confusion complicated by marked restlessness and hallucinations. It tends to occur mainly in the age groups above 50 years and almost only in males. The majority of the disturbances last only 1 week. The pathology found is primarily meningitis, followed by diffuse cerebral and vascular findings. The causes are predominantly infectious conditions. In a relatively high number of cases no cerebral pathology can be found.

V. *Prolonged drowsiness* affects most often the younger age group up to 50 years, and occurs in males as often as in females. The duration is usually several weeks. The pathology is vascular, diffuse cerebral, and neoplastic in nature, followed in some instances by meningitis and brain abscess. The causes are neoplastic, infectious, toxic, aneurysms, and miscellaneous. Although the localization of focal lesions is scattered over all brain regions, there is a slight predilection for the left temporo-parietal lobe and the basal ganglia.

VI. *Fluctuating levels of consciousness* occur when a patient fluctuates at short intervals between various stages of disturbed consciousness. Though the number of cases in this group is small, it is evident that the predilection age is from 40 to 60 and that females are more frequently affected than males. There is no characteristic duration for the disturbance, which may be short or long. The pathology reveals a high incidence of vascular lesions, followed by various other groups of findings. The causes are either neoplastic or of endocardial origin or infections. The localization shows a trend towards avoidance of the hemispheres, as the lesions are apt to occur in the basal ganglia or in more caudal parts of the brain.

VII. *Prolonged aphasia.* This category includes all cases of aphasia, although a classical motor aphasia does not constitute a disturbance of consciousness. Since pure cases are rare and the great majority of aphasias have, in addition to the motor, some sensory disturbances, it was thought permissible to list these findings together. The occurrence is highest from 40 to 70 years, and males are more often affected than females. The duration shows no characteristic tendency and may be weeks, months, or years. The pathology found is mainly of vascular origin, followed by tumors and diffuse cerebral findings, meningitis, and abscess. The causes of aphasia are primarily neoplasms, infections, and arteriosclerosis, followed by endocardial, miscellaneous, and toxic conditions. The localization of focal lesions shows the known predilection for the left frontal and left temporoparietal regions.

VIII. *Prolonged stupor* encompasses all conditions with apathy and lack of interest in the surroundings. It is an intermediate stage between drowsiness and semicoma, and is clinically characterized by the patient's ability to keep body position in absence of any verbal manifestations. Predilection age is the sixth decade. Females suffer from this disturbance more than males. The duration is usually a matter of weeks, although it may last a few months. The pathology is primarily vascular, followed by tumors, diffuse cerebral pathology, meningitis, and tumors. This disturbance has also a relatively high incidence of cases in which no findings, or arteriosclerosis only, could be found. The causes are of neoplastic and arteriosclerotic nature, followed by infectious, toxic, miscellaneous conditions, and aneurysms. No predilection of localization can be recognized.

IX. *Prolonged semicoma and coma* are states of irresponsiveness in which the sensory processes seem to be disturbed and usually combined with changes in respiration, pulse, blood pressure, and temperature. They occur at all ages, but the highest frequency is found in the age groups of 50 to 70 years. They occur more frequently in women than in men; their duration is primarily one of a few days to two weeks. Nevertheless, cases

have been found in which the semicoma lasted for months. The pathology is primarily vascular, followed by tumors, diffuse cerebral findings, meningitis, and abscess. The distribution of the localized lesions shows no predilections for any brain region.

X. *Prolonged confusion following or preceding convulsions.* This category includes all cases which had confusional episodes of several days' duration before or after convulsions. The group is too small to draw definite conclusions.

XI. *Repeated episodes of confusion* are characterized by periods of confusion which are interrupted by lucid intervals of weeks' or months' duration. They seem to occur predominantly in old people. Males are affected more than females. The pathology is of vascular and diffuse cerebral character. Arteriosclerosis is the predominant cause. The basal ganglia seem to be affected more often than other brain regions.

XII. *Repeated loss of consciousness without convulsions* refers to cases suffering from repeated, usually sudden, losses of consciousness, lasting from a few minutes to several hours or days. This disturbance occurs most frequently between the ages of 30 and 70 and in females. The pathology is primarily vascular, followed by diffuse cerebral findings and ultimately by tumors, meningitis, and abscess. The left temporo-parietal region and the basal ganglia seem to be affected more often than other brain lesions.

XIII. *Repeated loss of consciousness associated with convulsions* describes cases with generalized or Jacksonian fits accompanied by loss of consciousness. It occurs at all ages but, in contrast to other disturbances, it is also found in many children. Males and females are equally affected. The pathology consists of tumors and diffuse cerebral findings, whereas meningitis, vascular lesions and abscesses are rare. The causes are predominantly of neoplastic and infectious nature. The localization of focal lesions seems to involve primarily both frontal, temporal, and parietal regions.

All cases. Seventeen per cent of 1682 cases verified by autopsy have either a prolonged or repeated disturbance of consciousness. Though scattered through all the age groups, the highest frequency of cases can be found between 50 and 70. Males are more frequently affected than females, as indicated by a ratio of 3 to 2. The pathology found is, in decreasing order of frequency, vascular, neoplastic, diffuse cerebral, meningitis and abscess; findings in arteries only and absent pathology occur in a very small percentage of cases. The localization shows that the frontal and the temporo-parietal regions, as well as the basal ganglia, are more often affected than other parts of the brain.

Cases with no cerebral pathology. Out of the 286 cases, there were only 9 (3 per cent) which had no cerebral findings; 8 of these were over 50 years of age. The disturbances of consciousness were all of the prolonged type: 2 cases of delirium, 3 cases of confusion, 2 cases of stupor, one case of intellectual impairment, and one with fluctuating levels of consciousness comprised the 9 cases. The conditions in which these disturbances occurred were: septicemia (2 cases), uremia (1 case), multiple abscesses (1 case), toxic goiter (1 case), bleeding duodenal ulcer (1 case), pulmonary emphysema (2 cases—one due to bronchiolitis and one due to pulmonary thrombosis), and fat necrosis of the pancreas (1 case).

Cases with no intracerebral pathology but with generalized or cerebral arteriosclerosis. In 12 out of 286 cases (4 per cent) no intracerebral pathology could be found; 10 of these, however, had cerebral arteriosclerosis; 9 had generalized extracerebral arteriosclerosis. Except for one case, all were older than 48 years. The following disturbances of consciousness were present: Coma (3 cases), stupor (3 cases), convulsions (2 cases), drowsiness (2 cases), confusion (2 cases). The diseases found were: arteriosclerosis and hypertensive heart disease (2 cases), uremia (2 cases), pernicious anemia (2 cases), septicemia (2 cases), Simmond's disease, pyonephrosis, syphilitic aortitis, and kidney tumor, 1 case each.

Cases with a series of different disturbances of consciousness. Twenty-one out of 286 cases, or 7 per cent, had three or more successive, definite types of disturbances of consciousness. Intellectual impairment, drowsiness, confusion, aphasia, stupor, coma, and convulsions were combined in various ways. In most instances the disturbance started with obvious intellectual impairment or drowsiness of long duration, followed later by either

aphasia or confusion and stupor, sometimes combined with convulsions. The 21 cases consisted of 9 brain tumors, one case each of Schilder's and Alzheimer's disease, one case of encephalitis, one case of cerebral degeneration of unknown origin, 3 cases of meningitis, 3 cases of subdural hematoma, and 3 cases of other cerebral vascular lesions. The localization of the processes showed a scattered distribution over various brain regions.

Discussion

The present study was undertaken in order to determine the diagnostic value of a variety of disturbances of consciousness as they are met in a general hospital. The first part of this investigation was concerned with the search for a suitable method which would express in either qualitative or quantitative terms the degree of the various disturbances. Experience acquired in cases with artificially induced unconsciousness, as in shock therapy and anesthesia, led to the selection of 18 signs which were observed to be altered in the course of progressive unconsciousness. In order to establish the value of these signs in clinical conditions such as coma, stupor, confusion, and others, 49 patients were examined repeatedly and the results of these 72 examinations were reported. It could be demonstrated that there exists a uniformity of symptomatology regardless of the disease studied. A lawful sequence in the appearance and disappearance of signs of unconsciousness was found which corroborated observations made after epileptic and artificially induced convulsions.[9]

Analysis of the sequence and disappearance of certain signs in progressive cases of brain disease seems to have considerable diagnostic value and also sheds some light on the nature of unconsciousness. Since correct intellectual functioning necessitates the presence of the greater part of the cortex and hemispheres, failure in psychometric examinations would indicate that the first parts of the brain to suffer in diseases producing unconsciousness are the cortical regions. It seems to be more than coincidence that these parts of the brain are also the most sensitive to oxygen want.[41,42] The absence of changes in temperature, pulse, blood pressure, and respiration in this stage can be considered as supporting evidence that vital centers are not yet affected. In the next stage, defective memory, inability to undergo testing, and disorientation are associated with changes in vital signs, indicating that lower centers are involved. The more unconscious a subject becomes, the more mechanisms begin to fail. After the intellectual functions are severely disturbed, the nociceptive or higher reflexes begin to become defective, followed ultimately by abolition of tendon and eye reflexes. In the latter stage, changes in vital signs are the rule. This and the failing of the reflexes gives evidence of damage to vital subcortical centers since ordinary reflexes can usually be elicited in decorticated conditions.

Since the sequence of occurrence of signs of consciousness seems to be subject to a regular progression, one might attempt to formulate a more objective definition of the clinical terms used. Intellectual impairment should be reserved for conditions in which the signs listed in Fig. 1 are all present and in which psychological testing is necessary for demonstration of the defect. Confusion refers to states with impaired orientation; stupor, semicoma and delirium should be reserved for those instances in which, in addition to disorientation, the voluntarily controlled reflexes are disturbed, and coma finally should be used only when the subject shows absence of tendon and eye reflexes and does not react any more to call by name. From a diagnostic and prognostic standpoint, it becomes evident that the severer the disturbance of consciousness becomes, the smaller will be the chance for recovery (Fig. 1). Thus disappearance of higher and lower reflexes in cases with semicoma and coma, indicates approaching death.

The second part of this investigation was concerned with the accumulation of pathological data from cases who suffered during life time of prolonged or repeated disturbances of consciousness. The conclusions which can be drawn from clinical records and autopsy protocols are naturally subject to restrictions. The limitations are not to be seen in the neuropathological work up, which was done for the entire ten year period covered by Dr. C. S. Kubik, but rather in the description and accurateness of the history of the disturbance of consciousness. Since a number of physicians contributed case histories, it is probable that some paid more attention to the description of these phe-

nomena than others. The selection of autopsies possibly influenced the results, too, since the permission to perform a postmortem examination is not obtained in all cases. Nevertheless it was possible to outline characteristic features which should be useful in differential diagnostic considerations (see p. 77).

Some of the findings raise a number of questions. Drowsiness and convulsions, for instance, occur predominantly in young people, as opposed to confusion and intellectual changes found in older subjects. Whether this difference is due to the type of disease afflicting the various age groups or due to a different reaction of the aging brain is difficult to decide. The diffuse atrophy of the brain present in older subjects finds its clinical equivalent in decline of the learning functions.[43] The older individual might be described psychologically as being at the upper limit of his resources. Intellectual deficiency thus becomes apparent immediately after a lesion develops in a brain afflicted already by involutional changes, whereas in young people a proportionately greater lesion may be necessary to produce intellectual changes. Hormonal influences in the aging brain are indicated by the differences found in the two sexes. Delirium, confusion and intellectual changes occur more often in males; coma, repeated coma and stupor are found more often in females. The low incidence (3 per cent) of cases without intracranial pathology indicates that a history of repeated or prolonged disturbances of consciousness is almost always a sign of irreversible brain lesions. An exception should be granted the cases of idiopathic epilepsy which were represented in this series by a small number only. Patients with prolonged confusion, intellectual changes and convulsions show a high incidence of diffuse cerebral pathology. It follows that psychological testing and accurate mental examination should be especially valuable in these cases, furnishing supportive evidence of brain damage.

Some of the figures given in this paper differ to a certain extent from statistics of state hospitals.[44] The tabulation of the causes in our study reveals that neoplastic and infectious conditions are more frequent than arteriosclerotic ones. This difference can easily be explained considering the restricted type of diseases treated in mental institutions, compared to the variety of autopsies in a general hospital.

The tabulation of the localized lesions indicates no remarkable predilection except for the group of aphasias. The majority of disturbances have lesions within the frontal, temporal, or parietal regions, or in the basal ganglia. Although this may, on the one hand, suggest that unconsciousness occurs more frequently in lesions of the hemispheres, it may, on the other hand, express the frequency of brain pathology in general. Vascular lesions are certainly more frequent within the distribution of the anterior and middle cerebral arteries than elsewhere; gliomas, especially glioblastoma multiforme, are also found in those areas. Disturbances of consciousness, therefore, seem to be associated with almost any pathology occurring in a variety of brain regions. In 3 per cent of all the cases no intracranial lesions were found and 4 per cent had cerebral or generalized arteriosclerosis only. Hence it is safe to assume that, in addition to the brain lesion almost always present, other factors of pathophysiological nature must contribute to the development of unconsciousness. In reviewing the cases, one had the impression that the extent of the damage is of greater importance than any other factor. The degree of consciousness, therefore, would seem to depend on the amount of normal functioning brain tissue left. Whenever a lesion or an abnormal chemical process affects the brain to a considerable, even though unknown, extent, the organism becomes unresponsive to a variety of stimulations. Lesion is defined as a grossly or microscopically visible abnormality of tissue. Thus unconsciousness appears to be almost always a histogenic or chemogenic disorder.[22] Beginning with defective intellectual reactions, gradually or suddenly more and more functions fail until deep unconsciousness or death occur. Knowledge and recognition of a disturbance of consciousness seems therefore to help in establishing the type and extent of cerebral involvement in a variety of diseases.

Summary

1) The present paper deals with a study of disturbances of consciousness based on the repeated clinical examination of 49 patients

and on a review of 286 cases in which a complete postmortem examination of head and brain had been performed.

2) The 18 clinical criteria, used to determine the responsiveness of patients, belonged to four distinct groups: (1) higher intellectual functions; (2) orientation; (3) reflexes controlled by voluntary action; (4) tendon and eye reflexes. A uniformity of symptomatology and a rather typical sequence in number and character of signs involved in progressive disturbances of consciousness could be demonstrated, regardless of the disease studied. A more objective definition of conditions, such as coma, semicoma, stupor, confusion, delirium and intellectual impairment, has been suggested, based on the number and the type of signs observed.

3) Age and sex frequencies, duration of the conditions, neuropathologic diagnoses, causes of the disease, and localization of the brain lesions were discussed for the following repeatedly occurring or prolonged (longer than 72 hours) disturbances of consciousness: intellectual impairment, intellectual and personality changes, confusion, delirium, drowsiness, cases with fluctuating levels of consciousness, aphasia, stupor, semicoma and coma, confusion following or preceding convulsions, repeated episodes of confusion, repeated loss of consciousness without convulsions, and repeated loss of consciousness associated with convulsions.

4) Seventeen per cent of all the cases having an autopsy suffered from prolonged or repeated disturbances of consciousness. All but 8 per cent had intracerebral or meningeal lesions. In 4 per cent findings were present in the arteries only and in another 3 per cent no intracranial pathology could be found. Prolonged and repeated disturbances of consciousness occur most frequently in the sixth and seventh decade; males are more often affected than females as evidenced by a ratio of 3 to 2.

5) In conclusion, it can be said that when a prolonged or a repeated disturbance of consciousness occurs, cerebral lesions must be expected. Neuropathology, cause, and localization vary with the type of disturbance encountered and significant diagnostic differences have been described.

The author gratefully acknowledges the assistance and cooperation rendered by Dr. T. B. Mallory, director, and Dr. C. S. Kubik, neuropathologist of the Massachusetts General Hospital for making available the autopsy protocols on which this study is based.

References

1 Miller, J. G.: *Unconsciousness*, p. 329. John Wiley & Sons, New York, 1942.

2 Bissell, W. W., and Le Count, E. R.: "The Relative Frequency of the Various Causes of Coma," *J. A. M. A.*, 68: 500-501, 1917.

3 Bissell, W. W., and Le Count, E. R.: "A Consideration of the Relative Frequency of the Various Forms of Coma," *J. A. M. A.*, 64: 1041-1045, 1915.

4 Holcomb, B.: "Causes and Diagnosis of Various Forms of Coma," *J. A. M. A.*, 77: 2112-2114, 1921.

5 Solomon, P., and Aring, C. D.: "The Cause of Coma in Patients Entering a General Hospital," *Am. J. Med. Sc.*, 188: 805-811, 1934.

6 Solomon, P., and Aring, C. D.: "A Routine Diagnostic Procedure for the Patient Who Enters the Hospital in Coma," *Am. J. Med. Sc.*, 191: 357-361, 1936.

7 Solomon, P., and Aring, C. D.: "The Differential Diagnosis in Patients Entering the Hospital in Coma," *J. A. M. A.*, 105: 7-12, 1935.

8 Wolff, H. A., and Curran, D.: "Nature of Delirium and Allied States," *Arch. Neur. Psych.*, 33: 1175-1215, 1935.

9 Purves-Stewart, J.: "An Introduction to the Study of Delirium and Coma," *Med. Press*, 428-429, 1940.

10 Bailey, K. C.: "Confusional Mental States and Stupor," *Med. Press*, 442-444, 1940.

11 Hill, T. R.: "Delirium and Coma in Cardiovascular Disorders," *Med. Press*, 436-438, 1940.

12 Garland, H. A.: "Delirium and Coma in Infections and Neoplasms of the Brain," *Med. Press*, 436-438, 1940.

13 Oakley, W.: "Delirium and Coma in Diabetes and Uremia," *Med. Press*, 429-433, 1940.

14 Denny-Brown, D., and Russell, W. R.: "Experimental Cerebral Concussion," *Brain*, 64: 93-164, 1941.

15 Northfield, D. W. C.: "Delirium and Coma in Head Injuries," *Med. Press*, 433-436, 1940.

16 Ruesch, J.: "Intellectual Impairment in Head Injuries," *Am. J. Psych.*, 101, 1944.

17 Ruesch, J., and Moore, B. E.: "Measurement of Intellectual Functions in the Acute Stage of Head Injury," *Arch. Neur. Psych.*, 50: 165-170, 1943.

18 Nielsen, J. M.: *Agnosia, Apraxia, Aphasia*, p. 210. L. A. Neur. Soc., Los Angeles, 1936.

19 Roe, A., and Shakow, D.: "Intelligence in Mental Disorder," *Ann. N. Y. Acad. Sc.*, 62: 361-490, 1942.

20 Jahrreiss, W.: *Storungen des Bewusstseins, Handbuch der Geisteskrankheiten*, pp. 601-661. Julius Springer, Berlin, 1928.

21 Penfield, W.: "The Cerebral Cortex in Man: I. The Cerebral Cortex and Consciousness," *Arch. Neur. Psych.*, 40: 417-442, 1938.

22 Cobb, S.: *Foundations of Neuropsychiatry*, p. 231. Williams and Wilkins Co., Baltimore, 1941.

23 Cobb, S.: *Borderlands of Psychiatry*, p. 166, Harvard University Press, Cambridge, 1943.

24 Bleuler, E.: *Textbook of Psychiatry*, p. 634. MacMillan Co., New York, 1924.

25 Beecher, H. K.: *The Physiology of Anesthesia*, p. 388. Oxford University Press, New York, 1938.

26 Cohen, L. H.: "Return of Cognitive Conscious Functions After Convulsions Induced with Metrazol," *Arch. Neurol. Psych.*, 41: 489-494, 1939.

27 Proctor, L. D., and Easton, N. L.: "An Unusual Case of Prolonged Coma in Hypoglycemic Shock Treatment," *Am. J. Psych.*, 99: 203-209, 1942.

28 Goldfarb, W.; Bowman, K. M., and Wortis, J.: "The Effect of Alcohol on Cerebral Metabolism," *Am. J. Psych.*, 97: 384-387, 1940.

29 Himwitch, H. E.; Bowman, K. M., and Fazekas, J. F.: "Prolonged Coma and Cerebral Metabolism," *Arch. Neur. Psych.*, 44: 1098-1101, 1940.

30 Himwitch, H. E.; Bowman, K. M.; Daly, C.; Fazekas, J. F.; Wortis, J., and Goldfarb, W.: "Changes in Cerebral Blood Flow and Arteriovenous Oxygen Differences During Insulin Hypoglycemia," *Proc. Soc. Exp. Biol. Med.*, 45: 468-469, 1940.

31 Himwitch, H. E.; Bowman, K. M.; Fazekas, J. F., and Goldfarb, W.: "Temperature and Brain Metabolism," *Am. J. Med. Sc.*, 200: 347-353, 1940.

32 Wortis, J.; Bowman, K. M., and Goldfarb, W.: "Human Brain Metabolism," *Am. J. Psych.*, 97: 552-565, 1940.

33 Gibbs, F. A.; Davis, H., and Lennox, W. G.: "Electroencephalogram in Epilepsy and in Conditions of Impaired Consciousness," *Arch. Neur. Psych.*, 34: 1133-1148, 1935.

34 Lennox, W. A.; Gibbs, F. A., and Gibbs, E. L.: "The Relationship in Man of Cerebral Activity to Blood Flow and to Blood Constituents," *J. Neur. Psych.*, 1: 211-225, 1938.

35 Lennox, W. A.; Gibbs, F. A., and Gibbs, E. L.: "Relationship of Unconsciousness to Cerebral Blood Flow and to Anoxemia," *Arch. Neur. Psych.*, 34: 1001-1013, 1935.

36 Borowsky, M. L.: "Der Blinzelabwehrreflex, sein biologisches Wesen und seine Veranderungen als neues Symptom bei Hemiplegie," *Dtsch. Z. Nervenheilk*, 110: 134-150, 1929.

37 Snell, A. C.: "Optokinetoscope," *Trans. Am. Acad. Ophth.*, 44: 396, 1939.

38 Fox, J. C., and Holmes, A.: "Optic Nystagmus and Its Value in the Localization of Cerebral Lesions," *Brain*, 49: 333-371, 1926.

39 Stenvers, H. W.: "Uber die Bedeutung des optischen Nystagmus fur die cerebrale Diagnostik," *Schweiz. Arch. Neur. Psych.*, 14: 279-288, 1924.

40 Wells, F. L., and Ruesch, J.: *Mental Examiner's Handbook*, p. 122. Psychological Corporaation, New York, 1942.

41 Drinker, C. K.: *Carbon Monoxide Asphyxia*, p. 133. Oxford University Press, New York, 1938.

42 Van Liere, E. D.: *Anoxia, Its Effect on the Body*, p. 269, University of Chicago Press, 1942.

43 Wertham, H.: *The Brain as an Organ*, p. 538. Macmillan, New York, 1934.

44 Dayton, N. A.: *New Facts on Mental Disorders*, p. 486. C. C. Thomas, Baltimore, 1940.

45 Galant, S.: "Reflexus cochleo-palpebralis und Ober-Lidschlagreflex," *Arch. ges. Physiol*, 176: 221-222, 1919.

Are You A Subscriber?

If not, read through this issue. You will enjoy it, we know.

Then, if you would like more of the same practical articles, turn back here and use this convenient blank to enter your subscription.

SEND NO MONEY

PHYSICIANS POSTGRADUATE PRESS **Subscription Dept.**

Please enter my subscription to DISEASES OF THE NERVOUS SYSTEM for one year, for which I agree to pay $2.50 upon receipt of invoice.

Name_____

Street or Bldg._____

City_____ State_____

Delvinal Sodium Vinobarbital in the Treatment of Epileptic States*

EUGENE DAVIDOFF, M.D., *and* GEORGE M. DOOLITTLE, M.D.
Sonyea, New York

In previous communications the rapid sedative effect of Sodium 5 ethyl 5 (1 methyl 1 butenyl) barbiturate (delvinal sodium vinobarbital**) has been reported. This barbiturate appeared to be of value in treatment of acute toxic and infectious conditions; in convulsive disorders; in agitated patients; in psychoneurotics and in continuously disturbed cases, particularly of the manic depressive variety. Since it produced relatively fewer toxic sequelae, larger initial doses were used. Tolerance to "delvinal" sodium usually did not develop rapidly.

It also appears that delvinal is rapidly destroyed in the body. In urinary excretion tests using the Koppanyi method, we found that following the ingestion of as high as 10½ grains of delvinal sodium vinobarbital, none of this barbiturate was recovered in the urine.

Delvinal sodium vinobarbital, therefore, possessed some value in the treatment of mental states in which increased psychomotor activity was a predominating symptom. The rate of induction of sedation was very rapid. In smaller therapeutic doses it usually caused fewer toxic effects and less continued drowsiness than other barbiturates. Therefore, it can be used in place of or in combination with other sedatives or anti-convulsants.

Preliminary studies indicated that patients with convulsive disorders responded fairly well. At the Clinic of Syracuse Psychopathic Hospital, ten patients under 20 years of age who suffered from epilepsy of the mild type were given, orally, 1½ grs. of delvinal sodium, three times daily. All of these patients had seizures for from one to two years and had previously received phenobarbital. Of these, six were seizure free for one year after the administration of delvinal sodium. Of ten alternately chosen cases who received dilantin, four were seizure free during a one-year period but in three cases the administration was interrupted because of toxic effects.

Seventeen other more severe cases who had previously received dilantin were given dilantin and delvinal. Whereas improvement was noted in 7 of the 17 cases when dilantin was given alone, 12 of these 17 cases improved after delvinal sodium was added. Furthermore, since this procedure permitted a decrease in the dosage of dilantin, fewer toxic effects were noted.

Ten of these cases then received delvinal alone. Two of these did better on delvinal alone, six reacted better to delvinal and dilantin and two reacted better to dilantin alone.

As a result of these earlier observations, we decided to employ delvinal sodium in a series of 40 severe epileptics at Craig Colony who had previously received other medications and had not responded. These cases were predominantly of the grand mal type. They all had been ill for more than 2 years. Five were under 16 years of age; five were under 20 but over 16 years, and 30 were over 20 years but less than 50 years of age.

After a transition period of 2 weeks, delvinal sodium vinobarbital was administered to these for a three months' period. The dosage varied from 1½ to 3 gr. given three times daily. The seizure record of the patients for the three months' period prior to the use of delvinal was compared with the seizure record for the three months' period during which delvinal was employed. In a similar manner, comparative observations were also made on the mental status of the patients, with respect to their alertness, emotional reactions, coordination and ability to adjust to hospital routine and manual tasks.

Discussion of Results

In the accompanying table, the results obtained with respect to seizures and mental status in these chronic epileptic patients are indicated. Only 3 of the 40 subjects became seizure free and these were individuals who had relatively few convulsive manifestations in the preceding three months' period and two of these were under 20 years of age.

However, in 15 of the patients the seizures

*From the records of Craig Colony, Sonyea, New York.

**This preparation is manufactured by Sharp & Dohme, Inc., Philadelphia, Pa.

were markedly decreased and in 7 they were moderately decreased so that 22 of the 40 patients showed some improvement in regard to the convulsive manifestations. The seizures in 8 of the 40 cases were appreciably increased. In 10 of the cases the number of seizures showed no noteworthy decrease or increase. Five of seven cases with so-called symptomatic epilepsy due to definite organic causes responded well. The administration of delvinal sodium was discontinued in patients 21 to 40 (see accompanying table) after the three months' period had elapsed and these subjects were then given their previous medication for a subsequent three months' period. Patients 21 to 30 all experienced increase in seizures. In patients 32, 36, 37, 39 and 40 there was no appreciable change in the seizure record.

More favorable results were obtained in regard to the mental status of patients especially with respect to alertness and lack of drowsiness after the effects following the initial period of administration had subsided and the appropriate dosage was arrived at. Thirty-two of the patients showed a definite improvement in their mental status. Five remained unchanged and three became worse. The three patients who reacted poorly had transitory periods of confusion which soon disappeared after delvinal was discontinued. They had previously manifested the same reaction while receiving other barbiturates. One of these responded well when the drug was re-administered subsequently. Except for confusion and initial drowsiness no other untoward effects were noted.

Delvinal sodium was particularly effective in diminishing the number of serial seizures. The psychological after-effects such as psychomotor phenomena and confusion which usually followed these seizures were also considerably lessened. These results are illustrated in cases 5, 6, 7, 8, 9, 10 and 30 in the accompanying table. The administration of 5 grs. delvinal sodium intravenously caused the cessation of status epilepticus almost immediately in three cases.

In evaluating the results, psychogenic factors must be taken into consideration. None of the barbiturates or anti-convulsant drugs in themselves alleviate the number of seizures in chronic epileptics to any marked extent. Frequently, however, they render the patient more amenable to psychotherapeutic procedures and reorganization of their habit life with subsequent diminution of the number and severity of seizures.

While the results following the administration of delvinal sodium are not too impressive from the standpoint of rendering patients seizure free it must be remembered that almost all these individuals had manifested symptoms of epilepsy for a long period of time. They were all classed as severe types of epilepsy, had not responded to other anti-convulsant medications, and many of them had showed signs of deterioration. However, delvinal sodium vinobarbital is a valuable adjunct in rendering this type of patient more cooperative and amenable to psychotherapy.

Summary

The field of usefulness and advantages of delvinal sodium vinobarbital in the treatment of epilepsy may be summarized as follows:

1) In early and mild cases observed in outpatient clinics such as those of the petit mal variety, it is more effective than phenobarbital in controlling the seizures. Delvinal sodium acts more rapidly and does not produce the degree of drowsiness which follows the continued administration of phenobarbital.

2) Institutionalized patients who do not respond well to phenobarbital react better to delvinal sodium.

3) Because of its effect on psychomotor activity it is a valuable adjunct to other anti-convulsant drugs such as dilantin in the treatment of grand mal or severe motor seizures.

4) In institutionalized epileptics of the severe type, while the seizures are not greatly diminished, the most striking effect of delvinal sodium is on the mental status. A large percentage of patients were more alert, reacted better to hospital routine and did not manifest drowsiness. Except for the three patients mentioned, confusion and toxic effects were less evident after continued administration when delvinal sodium was employed.

5 Because of its rapid action and relatively low toxicity, the oral administration of delvinal sodium is of definite value in the treatment of serial seizures and their mental sequelae.

6) None of the barbiturate derivitives in themselves alleviate the total symptomatology in chronic epileptics except as an adjunct to other procedures.

SEIZURES

	Before Delvinal	*During Delvinal Administration*	*Increase or Decrease of Seizures*	*Mental Status*
1. F. B.	6	0	−6	Improved
2. C. F.	5	0	−5	Improved
3. H. F.	3	0	−3	Worse
4. D. L.	6	1	−5	Improved
5. M. H.	11 (3 serial)	1 (none)	−10	Improved
6. J. C.	20 (2 serial)	5 (none)	−15	No change
7. E. Z.	42 (7 serial)	3 (1 serial)	−39	Improved
8. A. B.	125 (4 serial)	11 (none)	−114	Improved
9. W. C.	233 (12 serial)	14 (none)	−219	Improved
10. W. M.	90 (2 serial)	33 (none)	−57	Improved
11. W. E.	29	12	−17	Improved
12. S. S.	23	12	−11	Improved
13. D. N.	27	15	−12	Improved
14. J. M.	24	16	−8	Improved
15. P. P. (a)	17	9	−8	Improved
16. J. B.	26	20	−6	Improved
17. L. B.	12	7	−5	Improved
18. J. G.	20	15	−5	Improved
19. M. S.	9	5	−4	Improved
20. H. A.	7	4	−3	Improved
21. P. P. (b)	13	10	−3	Improved
22. D. G.	12	9	−3	No change
23. F. K.	6	4	−2	Improved
24. M. S.	12	11	−1	Worse
25. G. S.	10	9	−1	Improved
26. J. K.	8	7	−1	Improved
27. R. B.	6	6	0	Improved
28. D. M.	7	7	0	Improved
29. H. W.	11	11	0	Improved
30. C. V.	94 (4 serial)	94 (1 serial)	0	Improved
31. N. B.	21	22	+1	Improved
32. C. F.	34	36	+2	Improved
33. I. N.	11	20	+9	No change
34. E. H.	2	11	+9	Improved
35. H. W.	31	42	+11	No change
36. K. C.	6	20	+14	Improved
37. P. L.	7	23	+16	Improved
38. L. B.	5	22	+17	Worse
39. T. M.	5	27	+22	No change
40. J. P.	25	67	+42	Improved

References

1 Cope, A. C., and Hancock, E. M.: "Substituted Vinyl Barbituric Acid. I. Isopropanyl Derivatives," *J. Am. Chem. Soc.*, 61: 96, (Jan.) 1939.

2 Davidoff, E.: "The Sedative Action of 'Delvinal' Sodium in Disturbed Psychiatric Patients," *Psychiat. Quart.*, 15: 370-379, (April) 1941.

3 Davidoff, E.: "The Use of Barbiturate Sedatives in Excited Mental Patients," *Dis. Nerv. Sys.*, 2: 288-290 (Sept.) 1941.

4 Davidoff, E., and Goodstone, G. L.: "A Comparative Study of the Effects of Three Barbiturate Compounds in Excited Psychotic Patients," *Med. Record*, Vol. 155, No. 1, pp. 22-26, (Jan.) 1942.

5 Hendrix, J. P.: "Studies of Two New Substituted Vinyl Barbituric Acids," *J. Pharm. and Exper. Therapy*, 68: 22, (Jan.) 1940.

Electroencephalographic Study During Epileptic Seizures Related to Hyperventilation

LEON J. ROBINSON, M.D.*
Palmer, Massachusetts

Introduction

The fact that in some epileptic patients seizures may be induced by hyperventilation was first reported by Rosett[1] and also by Foerster[2] in 1924.

During the pulmonary overventilation, the carbon dioxide content is reduced not only in the alveolar spaces but is also reduced in the blood. In 1928 Lennox[3] demonstrated that petit mal seizures can be temporarily abolished by breathing air containing an increased concentration of carbon dioxide. In 1940 Lennox, Gibbs and Gibbs[4] made an important contribution to the study of the relationship of carbon dioxide to the precipitation of seizures. They reported that when overventilation resulted in a seizure the latter was almost invariably a petit mal seizure or occasionally a psychomotor seizure, but that they had never observed a grand mal seizure to be so produced in several hundred trials. On the other hand, in two of their cases in which there were both petit mal and grand mal attacks, a grand mal seizure occurred when the patient resumed breathing room air after long-continued subjection to a high carbon dioxide atmosphere, which had stopped all petit mal activity as judged by the electroencephalogram. They found that patients with epilepsy showed an abnormal fluctuation both in arterial and in jugular venous carbon dioxide content, the values tending to be abnormally low in patients subject to petit mal seizures and tending to be abnormally high in patients subject to grand mal seizures, and tending to be either abnormally high or low in those having both grand mal and petit mal seizures. Repeated studies on single subjects showed that the carbon dioxide content might be normal at one time but grossly abnormal at another. Seventy per cent of their ninety-three epileptic patients had values above or below the normal range of 52.5 to 56 volumes per cent jugular venous carbon dioxide. They emphasized that the deviation from normal carbon dioxide values occurred without coincident shift in oxygen values, proving that the former were not simply a reflection of oxygen changes. They also correlated their electroencephalographic findings with the carbon dioxide content. In three patients who showed the alternately fast and slow waves which the same authors have previously identified with petit mal activity[5] the arterial carbon dioxide content over a half-hour period on a number of days was high when the electroencephalographic record showed less activity, and the carbon dioxide was low when the electroencephalographic record showed more activity, so that there was an inverse relationship between the arterial carbon dioxide content and the amount of petit mal activity.

Nims, Lennox and their associates[6] reported that patients with petit mal epilepsy responded to overventilation with a greater drop in the carbon dioxide content of the jugular vein and maintained the low level for a longer period after the hyperventilation had ceased than did the non-epileptic subject.

Hans-Werner found that of 100 epileptic patients only ten had a seizure as a result of hyperventilation.[7]

Cobb, Sargant, and Schwab discovered that some patients show spontaneous increases in breathing coincident with petit mal electrical activity.[8]

Present Study

The present study concerns an analysis of the electroencephalographic findings in 14 epileptic patients in whom hyperventilation induced a seizure.

The electroencephalographic criteria for abnormality constituted waves of six or less per second in frequency, wave and spike formation, or fast activity accompanying grand mal seizures.

Of 146 epileptic patients these 14, comprising 9½ per cent of the total tested, were the only ones to have a seizure during or following a six-minute period of hyperventilation. One hundred thirty-two patients (90½%) did not

*Monson State Hospital, Palmer, Massachusetts.

have a seizure related to hyperventilation.

Of the 14 patients in whom hyperventilation induced a seizure, there were three males and eleven females. The ages ranged from six years to forty years.

The clinical diagnosis was idiopathic epilepsy in 13 and epilepsy symptomatic of encephalitis in 1.

The family history was negative in 6 cases. There was a history of epilepsy in 2 cases, of a sibling with "fainting attacks" in one case, of migraine in 2 cases, of psychosis in 3 cases and one of the latter gave a history of mental deficiency.

The age of onset varied from 3 months to 30 years, the duration of the epilepsy from 3 months to 27 years. None of the patients had been seizure-free for more than 6 months prior to the recording.

The intelligence quotients ranged from 50 to 93 among the eleven cases in which it had been recorded.

Of the 14 patients who had a seizure related to hyperventilation the resting electroencephalogram was abnormal in 12 (85%), and was normal in 2 (15%). The electroencephalogram showed slow waves on hyperventilation in all 14 cases. Of the 12 with abnormal resting records 6 had one or more normal lead areas while other areas were abnormal. In one case the only abnormal area at rest, of five areas recorded, was the left motor area and on hyperventilation slow waves appeared also in the left occipital area. A second similar case was present among the 12 with abnormal resting records. Of the two cases in which the resting period was normal, one showed slow waves on hyperventilation from all of the three leads used, recording from the right side of the head; and the other showed slow waves on hyperventilation from the left leads, but not from the right leads.

There was a varied distribution of the spike and wave forms in the 14 patients. Two resting records contained spikes and waves (as well as slow waves), in one of which they persisted both during hyperventilation and petit mal seizures, and in the other of which they disappeared (leaving only the slow waves) during hyperventilation and petit mal seizure. Of 12 resting records free of spike and wave forms, four cases developed these (as well as slow waves) during both hyperventilation and petit mal seizures; and eight cases did not exhibit spike and wave patterns with the slow waves during either hyperventilation or seizures, the latter consisting of petit mal in 6 cases, of grand mal in one and of involuntary crying in one.

Of the 14 cases in whom seizures occurred, phase localization was carried out in five cases, four on one side and one on both sides, the latter showing out of phase foci on both sides and the remaining four showed no such foci.

The induced seizures were similar in every case to the patient's usual spontaneous seizures.

The seizures were petit mal in 12 and occurred in 11 on hyperventilation and in one after hyperventilation. The seizures were grand mal in one and occurred after hyperventilation.

In one case there was no seizure but instead involuntary crying followed the hyperventilation, coincident with the appearance of slow waves on the electroencephalogram.

Of the 11 patients having a petit mal seizure during hyperventilation, in eight cases the seizure was induced by each new period of hyperventilation. The induced petit mal seizure occurred during the first five minutes of hyperventilation and often within the first three minutes. The patient having a petit mal seizure after hyperventilation had a seizure 2¼ minutes following hyperventilation. The patient having a grand mal seizure had his seizure 2½ to 4 minutes after the cessation of hyperventilation, the seizures occurring in twelve out of fifteen trials. The time relationship of seizures to hyperventilation was fairly constant for each case on each trial on the same or separate days.

The petit mal seizures were characterized for the most part by short loss of consciousness; turning of the eyes to one side (either the right or left), and often turning the head to one side; occasionally fixing of the eyes in the midline; mild clonic movements of the jaw and/or extremities; and relatively prompt complete recovery. The duration of the petit mal seizures varied from 13 to 20 seconds. In one case a series of petit mal seizures occurred on each period of hyperventilation.

The seizure was considered a grand mal when the muscular movements of tonus and clonus were marked and sustained.

The electroencephalogram in seizures was abnormal in all 14 patients, showing waves

less than six as well as six per second in every case. In addition, spike and wave forms occurred in five cases, all of whose seizures were classified clinically as petit mal attacks.

The leads which showed slow waves on hyperventilation were usually the ones which showed abnormalities during seizures, but leads which were occasionally unchanged even on hyperventilation became abnormal during the seizure.

Of the 14 patients, 12 were receiving medication and 2 were not. Eleven patients were receiving phenobarbital, the dosage ranging from one to six grains daily. One patient received dilantin sodium 6 grains daily.

The two patients whose resting electroencephalogram was normal were receiving phenobarbital grains 1½ and grains 3, respectively, daily; and their intelligence quotients were 53 and 51. Their histories and related clinical data did not differ significantly from those of the 12 patients with abnormal resting electroencephalograms.

Comment

Since the reports of Rosett[1] and of Foerster,[2] it has been known that, in some epileptic patients, seizures may be induced by hyperventilation. That this effect of overventilation depends on the consequent decrease in blood carbon dioxide is indicated by the work of Lennox and his associates.[3,4,6]

The present study corroborates the important observation of Lennox and his associates that the type of seizure which can be induced by hyperventilation is primarily the petit mal seizure. In the present series of 14 patients in whom hyperventilation precipitated a seizure, 12 had petit mal seizures, only one had a grand mal seizure and one had an episode of involuntary crying. This study also demonstrated that for a given case the petit mal seizures occurred at a relatively constant time during the period of hyperventilation, and tended to be reproducible on each period of hyperventilation on the same or different days. The one grand mal seizure occurred 2½ to 4 minutes after the cessation of hyperventilation in twelve of fifteen trials. The induced seizures were similar to the patients' spontaneous seizures.

In the present series of cases hyperventilation induced a seizure in 9½ per cent of the epileptic persons tested, a result which agrees closely with Hans-Werner's figure of 10 per cent,[7] and which is appreciably lower than Rosett's figure of 40 per cent.[9]

In the diagnosis of epilepsy the hyperventilation test has the advantages of simplicity of application, and specificity of response when a seizure is induced. It enables the physician to observe the actual seizure pattern.

The hyperventilation test has the disadvantages of limited applicability as only a small percentage of patients develop a seizure on hyperventilation, and the necessity of active co-operation on the part of the patient. Satisfactory hyperventilation cannot be obtained in some patients with mental deficiency, deterioration, or senility. The test does not rule out bizarre hysterical episodes.

By contrast the electroencephalogram has the advantages of permanency of record, minimum degree of co-operation on the part of the subject, possibility of localizing a focus or circumscribed lesion, and wave forms which are often specifically diagnostic in themselves. The disadvantage is the non-specificity of the abnormal potentials occurring in some of the relatives of epileptics, in some persons with mental deficiency, psychoses or behavior disorders, and in cases of increased intracranial pressure.

The desirability of a period of hyperventilation during electroencephalography is obvious.

Summary

Of 146 epileptic patients 14 or 9½ per cent developed a seizure during or following a 6-minute period of hyperventilation. One hundred thirty-two patients or 90½ per cent did not have a seizure related to hyperventilation.

The diagnosis was idiopathic epilepsy in 13 cases and epilepsy symptomatic of encephalitis in one.

Of the 14 patients who had a seizure related to hyperventilation the resting electroencephalogram was abnormal in 12 (85%), was normal in 2 (15%). The electroencephalogram showed slow waves on hyperventilation during seizures in all 14 cases. The electroencephalograms in seizures showed waves of less than 6 as well as 6 per second in every case. In addition, spike and wave forms occurred in five cases, all of whose seizures were petit mal attacks.

The seizures were petit mal in 12 cases and

occurred in 11 on hyperventilation. The seizures were grand mal in one case and occurred after hyperventilation. In one case there was no seizure but instead involuntary crying.

The seizures which occurred on hyperventilation were similar to the patients' usual spontaneous seizures.

In contrasting the value of the hyperventilation test with the electroencephalogram in the diagnosis of epilepsy, it was concluded that though the hyperventilation test is more available, a positive response in the form of a seizure occurs in a more limited number of cases.

References

1 Rosett, J.: "The Experimental Production of Rigidity of Abnormal Involuntary Movements and of Abnormal States of Consciousness in Man," *Brain*, 47: 293, (Aug.) 1924.

2 Foerster, O.: "Hyperventilationsepilepsie," *Deutsche Ztschr. F. Nervenh.*, 83: 347, 1924-1925.

3 Lennox, W. G.: "The Effect on Epileptic Seizures of Varying the Composition of Respired Air," *J. Clin. Inv.*, 6: 23, 1928.

4 Gibbs, E. L.; Lennox, W. G., and Gibbs, F. A.: "Variations in the Carbon Dioxide Content of the Blood in Epilepsy," *Arch. Neurol. and Psych.*, 43: 223-239, (Feb.) 1940.

5 Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: "The Electroencephalogram in Diagnosis and in Localization of Epileptic Seizures," *Arch. Neurol. and Psych.*, 36: 1225-1235, (Dec.) 1936. "Epilepsy: A Paroxysmal Cerebral Dysrhythmia," *Brain*, 50: 377, (Dec.) 1937.

6 Nims, L. F.; Gibbs, E. L.; Lennox, W. G.; Gibbs, F. A., and Williams, D.: "Adjustment of Acid-Base Balance of Patients with Petit Mal Epilepsy to Overventilation," *Arch. Neurol. and Psych.*, 43: 262-269, (Feb.) 1940.

7 Hans-Werner, Jans: "Diagnostic Applicability of Some Methods to Induce Epileptic Attacks," *Arch. F. Psychiat.*, 106: 267-295, (March 5) 1937.

8 Cobb, S.; Sargant, W. W., and Schwab, R. S.: "Simultaneous Respiration and Electroencephalographic Recording in Petit Mal," *Tr. Am. Neurol. A.*, 65: 137-141, (June) 1939.

9 Cobb, S.; Sargant, W. W., and Schwab, R. S.: "Simultaneous Respiration and Electroencephalographic Recording in Petit Mal," In Discussion, Rosett, J.; *Tr. Am. Neurol. A.*, 65: 137-141, (June) 1939.

Neurological Clinical Pathological Conference

of the

Cincinnati General Hospital

CHARLES D. ARING, M.D., *Editor*

CASE 46907

Presentation

A 68 year old white male was admitted to the hospital on December 3. He had had dyspnea for many years, and in the years preceding his admission he had attacks of nocturnal orthopnea; these attacks were brought on also by excitement. He had ankle edema for some months. When seen at home just before admission to the hospital, he had auricular fibrillation and was given digitalis. Through oversight, the digitalis was not continued until two weeks after his admission to the hospital.

Examination and Course—On admission, the patient was overtalkative about himself and he seemed depressed. The heart was enlarged to the left and there was a loud, apical systolic murmur. The peripheral vessels were sclerotic; the blood pressure 155/110. On the second night after admission the patient got out of bed without permission. On December 8, the fifth hospital day, the patient became uncooperative and confused. He kicked at the window in his room and refused to eat. During the rest of his hospital stay, the patient remained confused, mute or noisy, and disoriented. He would occasionally recognize friends or relatives. On December 8 and until December 16 he was given 15 grains of sodium bromide three times daily. On December 13, the patient became involuntary and remained so. He began to have hallucinations after December 19.

At the time of neurological examination on December 16, the patient was uncooperative and uncommunicative. The discs were normal, the retinal vessels were sclerotic. The pupils were 4 mm. in diameter and reacted well to light. The corneal reflexes were equal. There was no facial weakness. The tongue protruded in the midline and was dry. The arms and legs were strong. The knee jerks were reduced; the plantar responses were flexor. He withdrew from painful stimuli. The pulse was weak and irregular. Some pustules were present on the face.

The bromide was discontinued; digitalis

and sodium chloride were prescribed. Sulfathiazole was begun on December 22; 5 grams were administered in the first 24 hours, 6 grams the next day, and 3 grams on each of the next two days. Thence it was given sporadically.

The patient began to complain of generalized abdominal pain on December 16. Because of the intermittent complaint of abdominal pain and the fever, a surgical opinion was obtained on December 28. There was no localized tenderness, rigidity, or mass, but he complained with any abdominal palpation. Rectal examination was normal. The surgeon thought the fever was of central nervous origin, the neurologist thought it was due to disease outside of the nervous system. The patient expired on December 30.

Laboratory Data—On December 4 an EKG revealed a tendency to left axis shift and auricular fibrillation. Absent T waves in the first three leads were thought to indicate myocardial damage. Two examinations of the urine revealed the specific gravity to be 1.022, an albumin content of 10 mg., qualitative tests for sugar were negative. Microscopic study of the urine showed an occasional red and white blood cell and a few hyaline casts. Analysis of the blood on admission revealed 4.5 million RBC, 7,500 WBC, and a hemoglobin of 14.2 grams; the differential count was normal. On December 28 the WBC was 12,100, the differential count was polymorphonuclear leukocytes 93 per cent, lymphocytes 3 per cent, monocytes 4 per cent. The blood Wassermann and Kline were negative. On December 17 the serum bromide was 50 mg. per cent. The blood sulfa level was 3.3 mg. per cent on December 28. On December 30 typhoid and paratyphoid agglutinations were negative.

A roentgen examination of the chest on December 24 revealed the heart to be moderately enlarged. The aorta was dilated and sclerotic. The lung fields were clear. On December 29 x-ray of the abdomen was negative.

On December 29 a lumbar puncture was done. The CSF pressure was 160 mm. of water. The protein content was 51 mg. per cent, there were 2 cells. The Wassermann was negative, and the gold curve was O^{10}.

The rectal temperature elevated progressively; from December 3 to 10, it ranged between 97.6 and 99.6; from December 10 to 17, between 98.8 and 100.6; from December 17 to 24, 100.2 to 103.6, and from December 24 to 30, 101.2 to 107 degrees F. The patient's temperature remained between 104 and 106 degrees during the last three days of his life.

Differential Diagnosis

Dr. Charles D. Aring: It seems likely that the diagnosis of this patient's neurological condition depends on a reasonably accurate analysis of the heart disease from which he suffered. He was 68 and had had heart disease probably for years and some degree of failure certainly for months at the very least. The nature of the heart disease appears to me to fall into one of two categories, either this failing heart was associated with hypertension or he had chronic rheumatic heart disease.

Some of the signs favor hypertensive heart disease. Statistically, failure is a common terminal event in hypertension; the left side of the heart is the most severely involved. A dilated and sclerotic aorta may pertain in hypertensive heart disease. In this case we have no information about the blood pressure over a period of time; it is known that the blood pressure was 155/110 on admission. The diastolic pressure was markedly increased; the systolic pressure may have fallen somewhat as the result of a failing heart. The systolic murmur may indicate mitral incompetency. Auricular fibrillation occurs occasionally in hypertensive heart disease. Another symptom that was present in this case and that may accompany hypertensive heart disease was abdominal pain. No note was made about the size of the liver, and it is assumed that it was not enlarged. The retinal arteries are usually narrow in hypertensive heart disease; they were sclerotic here. There was concommitant kidney damage. However, much the most important feature of the progress was the catastrophe a few days after admission to the hospital, the description of which would appear to indicate that a heart capable of producing emboli must be a main consideration.

Before attempting further to determine the nature of the condition, let us try to evaluate the psychological signs, and to localize the neurological disorder. Modern psychiatry teaches that psychological signs have little

localizing value in neurological diagnosis. Psychological signs stem from two basic factors: the personality structure and the disease. When psychiatric signs occur in the course of neurological disease, usually we do not allow ourselves to think that some portion of the cerebrum is involved. The confusional syndrome is not specific.

An effort will be made to localize the disease in the nervous system on the meagre evidence. If the neurological disease is predicated on heart disease, the lesions are most likely to be multiple. The only sign of localizing value might be the fever. The fever was unusually high and there was no associated leukocytosis or any other strikingly abnormal vital sign. Despite the fact that fever, as a rule, indicates infection, one thinks of hyperthermia and I suppose that the localization of one of the lesions may be in the hypothalamus. If so, the region about the supraoptic nuclei should be involved, damage to which may result in hyperthermia.

There is some negative evidence of localization. It seems to me that if the lesions were multiple, the so-called silent areas would have to be attacked since the patient was practically devoid of neurological manifestations. Therefore other localizations to be considered are the frontal lobes and the cerebellum, the latter particularly if the patient were rather ill and bedfast and not able to partake in the usual tests for cerebellar dysfunction.

If the nature of the lesion is embolic, emboli coming from the left heart usually lodge somewhere in the distribution of the middle cerebral arteries, on the left with a bit more frequency than on the right. So one might say that the patient may have had multiple cerebral lesions in the supraoptic region and possibly in the frontal and temporal lobes particularly in those portions supplied by the middle cerebral artery.

There are a few other points that might be mentioned. The abdominal pain might be the result of embolus to the abdomen (mesenteric or enteric).

Calculating from the bromide level in the blood, the patient could not have had more than 10 to 12 grams of bromide in his body on December 17. This amount would not appear to be significant as far as the symptoms were concerned, although this patient was in the age group where psychosis may be provoked by any noxa. The CSF is of no significance, except for the abnormal protein of 51 mg. per cent which may be seen in many diseases of the central nervous system.

It seems to me that the multiple lesions in and out of the nervous system indicate embolic phenomena so I should think that this man had rheumatic heart disease, and that emboli have lodged in the mesentery, kidney, and brain. The alternative is hypertensive encephalopathy.

Clinical Diagnosis

Fever of undetermined origin.

Possible pneumococcic peritonitis.

Generalized arteriosclerosis and arteriosclerotic heart disease.

Doctor Aring's Diagnosis

Multiple emboli in the brain, and in other organs, secondary to rheumatic heart disease.

Anatomical Diagnosis

Acute vegetative endocarditis with staphylococcus aureus, septicemia and metastatic abscess formation (brain, intestinal tract, kidneys, spleen).

Chronic rheumatic mitral valvulitis.

Congenital or acquired abnormality of the mitral valve.

Bronchopneumonia.

Discussion of Pathology

Dr. I. Mark Scheinker: Within the cortical ribbon there were diffusely scattered areas of cellular accumulation, which bore a relationship to the smaller vessels. Analysis of the lesions revealed that they were composed of leukocytes and in the center of the foci small capillaries were occluded by masses of organisms. We are dealing with bacterial emboli and consecutive miliary abscess formation. In the leptomeninges it is to be noted that most of the vessels are involved in the process. Hemorrhage was also found in the leptomeninges.

In other brain areas there was observed occluded capillaries surrounded by anemic infarction. Necrosis of tissue was caused by hypoxia of the perivascular area due to occlusion of small blood vessels.

Sections from the kidneys showed the same type of miliary abscess formation, as did sections taken from the intestinal tract. In the heart muscle small areas of cell accumula-

tion similar to those seen in the brain were found.

As Doctor Aring mentioned, we will have to look to the heart, especially the endocardium for the etiological agent. Here was found an old rheumatic valvulitis. The more acute lesions of endocarditis were superimposed on the old rheumatic heart disease.

A few words about the connection between heart disease and changes in the brain. Brain lesions in heart disease are common, in fact, they occur with more frequency than has been previously suspected. In 96 per cent of cases of heart disease Kernohan demonstrated lesions in the brain, with or without clinical manifestations. In 81 per cent of a large series of varying types of heart disease, Bodechtel found lesions widespread in the brain.

Dr. Aring: Were the lesions widespread in the brain?

Dr. Scheinker: I do not have too many sections, but what I have show widespread involvement of the brain. Localization cannot be exact in this case since the nervous system was examined first in the pathology department, and not until months later in the neuropathology laboratory.

Dr. Philip Wasserman:* I have very little to add to what Doctor Scheinker had demonstarted. There is one item that might illuminate the possible sequence of events in this case. A congenital or acquired abnormality of the mitral valve was found. Specifically, three separate and distinct leaflets, one of which was partially divided, could be seen. This may well have been a congenital anomaly and the rheumatic process could have developed on this original abnormality. Inasmuch as structural abnormality apparently predisposes to the secondary development of endocarditis, the recent staphylococcus vegetative formations in this case might have developed because of the presence of both the congenital abnormality and the old rheumatic process. I might say that the rheumatic process was quite advanced and that the mitral leaflets all showed typical stiffening and thickening. The chordae tendineae were also involved and were shortened and thickened. The acute vegetations were small and were present in two areas only, at the base of the auricle as a flat mural mass and along the free edges of the partially divided mitral leaflets as friable filiform structures. The latter vegetations incidently were present along the line of the partial division, as well as along the usual line of closure of the leaflets. The acute process was further indicated by roughening and reddening of the regional endocardium.

The acute vegetative endocarditis was, of course, responsible for the widespread metastatic abscess formations, abscesses being found in the kidneys, spleen, intestinal tract, and skin, as well as in the brain. These metastatic areas all appeared to be about the same age and all were obviously of recent origin. It might be mentioned that blood cultures taken at the time of the autopsy, as well as cultures taken from the spleen and kidney lesions all resulted in a growth of staphylococcus aureus.

Doctor Daniel Oscherwitz: Were the lesions in the nervous system old?

Doctor Scheinker: Apparently not older than two or three days; leukocytes usually disappear and are replaced by lymphocytes, and there were leukocytes still present in the brain lesions. We are dealing with a large number of small lesions disseminated throughout the brain, not large enough to produce focal symptoms, but evidently numerous enough to disturb mental function.

Doctor Aring: There are several inexplicable points in the case. This man had an overwhelming infection and yet did not have an increase in the white cells of the blood, although there was a polymorphonuclear content of 93 per cent. There were leukocytes and blood in the leptomeninges, and the fact that they did not register in the CSF is rather remarkable. One might expect cells in the CSF with the acute metastatic brain lesions associated with endocarditis.

Doctor Harry M. Salzer: The white blood count was done just two days before he died and the spinal puncture the day before death. Toone* in a study of 35 cases of acute and subacute bacterial endocarditis noted that 17 cases presented some cerebral signs or symptoms. In 11 of the 17 cases there was an excess of white blood cells in the CSF, ranging from 45 to 2450 per cm., and in others an occasional bloody CSF was found.

*Instructor in Pathology.

*Cerebral manifestations of bacterial endocarditis, Ann. Int. Med., 14: 1551-1574, 1941.

1944 Red Cross War Fund

When bombs fall there is no time to send help half way around the world. When a badly wounded fighting man needs a transfusion, it is too late to begin looking for a blood donor or find a nurse to care for him. When a lonely soldier learns of trouble at home, he needs help—immediately.

The American Red Cross provides that help wherever and whenever the need arises. A continuous procession of blood donors must be maintained, nurses must be recruited for the Army and Navy, trained Red Cross workers and supplies must be sent to camps, hospitals and foreign theaters of operation the world over.

When a train crash leaves scores injured, when flood engulfs a town, when epidemic strikes, delay may cost lives. Red Cross disaster relief and medical supplies, held in readiness for such emergencies, plus trained workers to rescue and assist victims and help in their rehabilitation, will prevent delay and thus save many lives.

To fulfill its many obligations to the armed forces and our people, the American Red Cross needs your help. During 1944 it must supply some 5,000,000 blood donations. Each month 2,500 nurses must be recruited for the Army and Navy. Red Cross field directors and other trained personnel must be stationed at military and naval posts and hospitals to help our fighting men and their families when personal trouble brews, a task in which the Red Cross chapter on the home front ably does its share.

At home the Red Cross must continue to maintain a state of alert. Disasters must be met as they occur. Nurse's aides and first aiders must be trained and other educational projects continued. Food parcels for distribution to prisoners of war must be packed, surgical dressings made and the thousand and one details of administering a far-flung, busy organization must be attended.

All activities of the American Red Cross are financed by voluntary gifts and contributions. During March, designated by President Roosevelt as Red Cross Month, the American Red Cross must raise its 1944 War Fund of unprecedented size to meet unprecedented needs. Your contribution will assure maintenance of all Red Cross services and help save many a life. Let's give!

Your RED CROSS is at his side

GENERAL INFORMATION

ORIGINAL ARTICLES only are published with the understanding that they are contributed exclusively to this Journal. Manuscripts offered for publication, correspondence relating to the editorial management and books for review should be sent to The Editor, DISEASES OF THE NERVOUS SYSTEM, University of Texas School of Medicine, Galveston, Texas. The publishers are not responsible for statements made or opinions expressed by contributors in articles published in its columns. All manuscripts are subject to editorial modification.

CUTS FOR ILLUSTRATIONS, DRAWINGS and CHARTS will be supplied without charge in moderate number, but special arrangements must be made with the editor and publishers for excess illustrations and elaborate tables.

REPRINTS are furnished on order only and must be requested of the publishers when galley proofs are submitted. Prices will be quoted at that time.

COPYRIGHTS cover publication in DISEASES OF THE NERVOUS SYSTEM and articles may not be reproduced without permission of the publishers.

BUSINESS CORRESPONDENCE regarding subscriptions, advertisements, and other business of DISEASES OF THE NERVOUS SYSTEM should be addressed to the publishers, Physicians Postgraduate Press, 500 North Dearborn Street, Chicago 10, Illinois.

CHANGE OF ADDRESS NOTICES should include the old as well as the new address.

PREPARATION OF MANUSCRIPTS

MANUSCRIPTS must be typewritten, double spaced, with good margins, on one side of the paper only. Send original copy to the editor, retaining a carbon.

DRAWINGS AND CHARTS must be made with BLACK INK to permit of best reproduction. Photographic prints of plates or slides on glossy paper produce the best halftones. Write the number of each illustration, drawing or chart on the back thereof together with the author's name and abbreviated title of the article.

LEGENDS FOR ILLUSTRATIONS, etc.: Typewrite list of same at end of manuscript with reference to number of illustration, drawing or chart.

BIBLIOGRAPHIES: Prepare carefully and fully to avoid confusion. Include in each reference (1) Number, (2) Author's last name followed by initials, (3) Title of article, (4) Name of periodical or book, (5) Volume, page and year if a periodical OR publisher if a book, viz.:

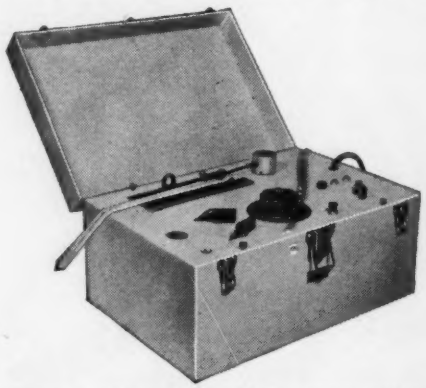
1. Bennett, A. E.: "Therapeutic Principles in the Care of the Psychoneuroses," **Dis. of N. S.**, 111: 2, 1942.

Place list of references at end of article, not in footnotes. Arrange in numerical order.

FULL ADDRESS of author should appear somewhere on manuscript, preferably at the end.

COSTEFF SANITARIUM
NERVOUS AND MENTAL DISORDERS
Shock Therapy (Insulin, Metrazol, Electroshock)
Home Environment
HARRY COSTEFF, M.D., *Psychiatrist*
1109 N. Madison Avenue—Peoria, Illinois
Telephone—4-0156

Garceau Electroencephalographs
NO BATTERIES — A. C. OPERATED
REQUIRE NO SHIELDING — INKLESS WRITING
PROMPT DELIVERY — SHIPPED READY TO RUN



THE JUNIOR GARCEAU ELECTROENCEPHALOGRAPH
A simplified inexpensive instrument for recording electrical potentials of the brain. Built-in interference eliminators permit use anywhere. Inkless records—no photography or film-development required. Instantaneous localization with any 2 of the 10 provided leads.
All Garceau Electroencephalographs operate entirely from the 115 volts, 50 or 60 cycle power lines.
Electro-Medical Laboratory, Inc.
Holliston, Massachusetts, U. S. A.

50 Beds **THE RETREAT, Inc.** Est. 1905
DES MOINES, 12, IOWA
For the diagnosis and treatment of Nervous and Mental Disorders in a homelike environment.
OCCUPATIONAL THERAPY, PHYSIOTHERAPY and SHOCK THERAPY
RUSSELL C. DOOLITTLE, M.D., *Medical Director* SYDNEY L. MACMULLEN, *Business Manager*
Member Central Neuro-Psychiatric Hospital Association

GLENSIDE
JAMAICA PLAIN, BOSTON, MASS.
• A small, attractively located sanitarium for nervous, mild mental or chronic illnesses. •
MABEL D. ORDWAY, M.D.
6 Parley Vale Tel. Jamaica 0044

SANITARIA DIRECTORY

The institutions listed in this section are among the finest private sanitaria in the United States. They are prepared to offer private, individual, specialized care to your patients.

BEVERLY HILLS SANITARIUM
Dallas, Texas

CHESTNUT LODGE SANITARIUM
Rockville, Maryland

COSTEFF SANITARIUM
Peoria, Illinois

COMPTON SANITARIUM and LAS CAMPANAS HOSPITAL
Compton, California

COYNE CAMPBELL SANITARIUM, Inc.
Oklahoma City, Oklahoma

ELMLAWN
(The Wilgus Sanitarium)
Rockford, Illinois

FENWICK SANITARIUM
Covington, Louisiana

THE FOREST SANITARIUM
Des Plaines, Illinois

GLENSIDE
Boston, Massachusetts

HARDING SANITARIUM
Worthington, Ohio

KENILWORTH SANITARIUM
Kenilworth, Illinois

LIVERMORE SANITARIUM
Livermore, California

NORTH SHORE HEALTH RESORT
Winnetka, Illinois

THE MARY E. POGUE SCHOOL
Wheaton, Illinois

RING SANATORIUM AND HOSPITAL, Inc.
Arlington, Massachusetts

ROGERS MEMORIAL SANATORIUM
Oconomowoc, Wisconsin

SAINT ALBANS SANATORIUM
Radford, Virginia

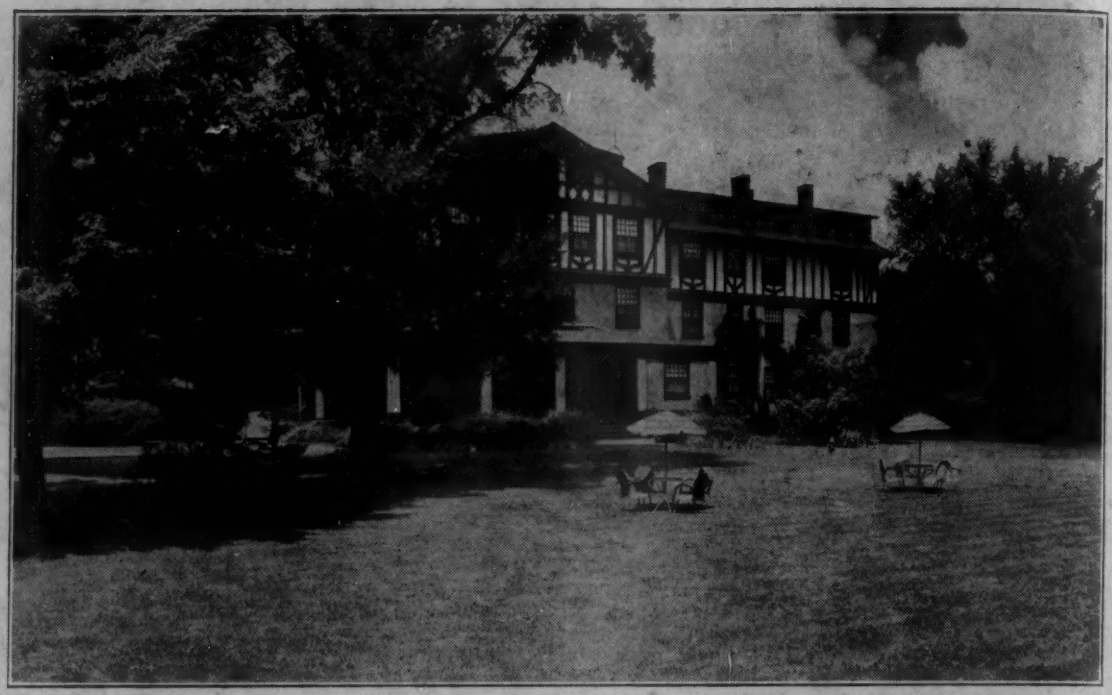
ST. JOSEPH SANITARIUM
Dubuque, Iowa

THE RETREAT
Des Moines, Iowa

THE STOKES SANITARIUM
Louisville, Kentucky

TUCKER HOSPITAL
Richmond, Virginia

WINDSOR HOSPITAL
Chagrin Falls, Ohio



Today It Is Treatment

Since the introduction of modern treatments for mental illnesses, sanitaria no longer properly belong in the class of custodial institutions. They should be, instead, centers of active medical treatment.

In keeping abreast with the progress in the psychiatric field, the KENILWORTH SANITARIUM has been among the first to adopt each of the modern methods of treatment for all types of nervous and mental illnesses.

So that today, the attending physician is offered here, facilities for use of the various modern treatments, accepted to date, with the full assurance of cooperation from an adequately experienced personnel.

ADDRESS OR PHONE, DIRECTOR,

Kenilworth Sanitarium

KENILWORTH, ILLINOIS

Telephone Wilmette 351 and 1662

MEDICAL STAFF

RESIDENT STAFF

EDWARD J. KELLEHER, M.D.
Director

RICHARD D. HUFF, M.D.
Associate

CONSULTANT STAFF

THOMAS L. FENTRESS, M.D.
HARRY R. HOFFMAN, M.D.
SAMUEL H. KRAINES, M.D.
WILLIAM J. NOLAN, M.D.